SCIENCE

JUNE 16, 1950

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AN ETHICAL CODE FOR SCIENTISTS
WARD PIGMAN AND EMMETT B. CARMICHAEL

CATALYSIS AND CARBONIUM IONS IN PETROLEUM FORMATION
BENJAMIN T. BROOKS

TECHNICAL PAPERS

COMMENTS AND COMMUNICATIONS

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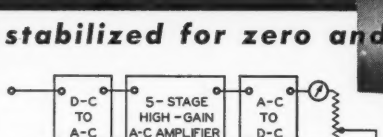

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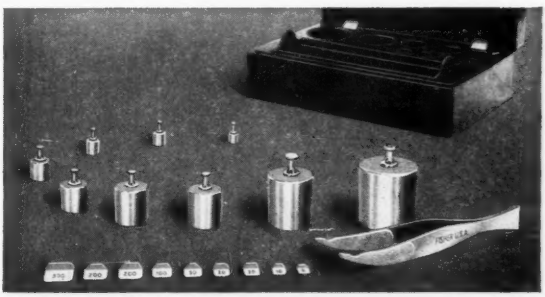

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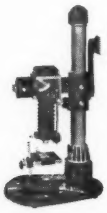

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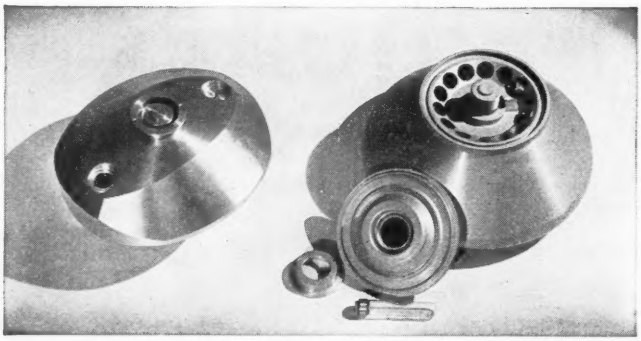

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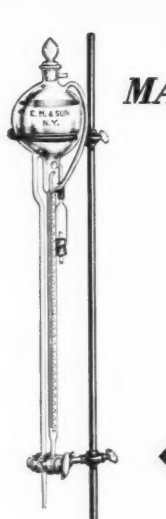

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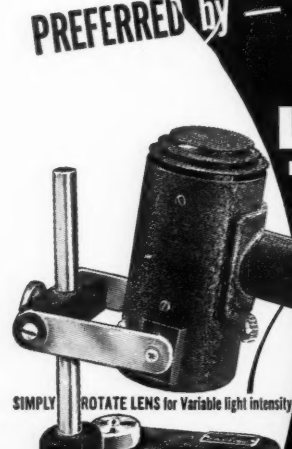

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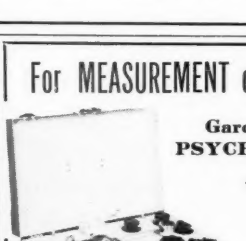

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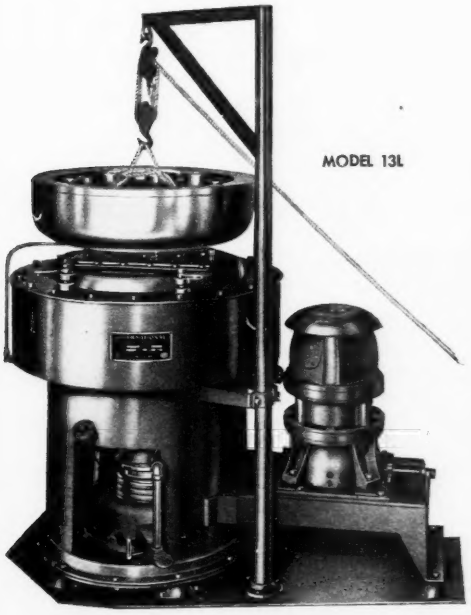

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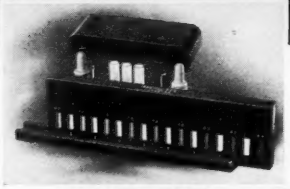

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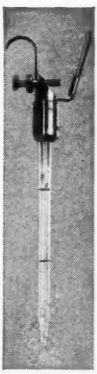

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An Ethical Code for Scientists

Ward Pigman and Emmett B. Carmichael

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A NEW PHENOMENON of our present-day society is the obviously important role played by science. Only a short time ago science was considered by many "practical" men as a plaything of inconsequential importance in contributing to the welfare of society. Although the significance of science was becoming more generally evident before World War II, this war demonstrated to the public in general and to legislators and businessmen in particular that science, especially basic science, is much more than a scholarly pursuit—that it is a vital force for the advancement or destruction of society. Science is now "big business." As a result, the scientist cannot and must not remain a scholarly recluse divorced from the remainder of society. His behavior and that of society toward him will greatly influence the progress of science and, to an increasing extent, that of society itself.

During its long period of development, science has evolved a code of professional tradition and ethics, largely in an unwritten form. This code, really the foundation of the scientific method in many of its aspects, has to a considerable extent been responsible for the achievements of science. Polanyi's (*12*) description of the effect of disregard for scientific traditions is applicable to many of our modern industrial and research organizations:

> Those who have visited the parts of the world where scientific life is just beginning, know of the backbreaking struggle that the lack of scientific tradition imposes on the pioneers. Here research work stagnates for lack of stimulus, there it runs wild in the absence of any proper directive influence. Unsound reputations grow like mushrooms: based on nothing but commonplace achievements, or even on mere empty boasts. Politics and business play havoc with appointments and the granting of subsidies for research. However rich the fund of local genius may be, such environment will fail to bring it to fruition.

The important achievements of science and its contributions to our civilization seem adequate proof of the basic validity of these traditions. On the other hand, conditions of scientific work have changed greatly, and obviously the traditions must be interpreted in terms of prevailing conditions. Science has emerged from a period in which the predominant effort was made by individuals, sometimes of almost an amateur status, to a period marked by the development of large research groups, many in the pursuit of research for profit. As a result, it is timely for the scientist to consider his professional traditions and to relate them in terms of the structure of modern scientific work.

These traditions are essentially an unwritten code of professional ethics. As pointed out by Leake (*9*), the term "professional ethics" as used generally includes the attitude of the individual scientist to society and to other scientists. It will be so used here. This concept of professional ethics inextricably involves social obligations, questions of etiquette, and adherence to accepted traditions. Claude Bernard (*1*) has contributed one of the better discussions of the ethical qualities needed in scientists, and the relationship of these qualities to the scientific method, although his remarks apply in the main to medicine and physiology.

Some of our professional organizations have established formal written codes of professional ethics.[1] In the medical field numerous papers and books have been written on the subject. One of the first extensive codifications was that of Percival (*9*) (1803), but the general precepts of Hippocrates (circa 500 B. C.) have modern acceptance. A major consideration at the first meeting of the American Medical Association in 1847 was the formulation of a code of professional ethics (*9*). The present code provides means for enforcement by its members. There has been some discussion of the professional responsibilities of industrial chemists (*6*) and a code has been proposed for this group (*7*). Scientific groups generally, however, have not formalized their traditions but have passed them on by example and by word of mouth as an informal part of the graduate student's training.

This failure of scientists as a group to consider ethics is revealed in the fact that *Chemical Abstracts*, since it was founded in 1907, listed only four refer-

[1] American Medical Association, *Principles of Medical Ethics* (*14*); American Dental Association, *Principles of Ethics* (*15*); American Association of University Professors, *Statements of Principle in Academic Freedom and Tenure* (*16*); American Institute of Chemical Engineers, *Constitution*, Article VIII (*17*); Engineers' Council for Professional Development, *Canons of Ethics for Engineers* (*18*). "The Geneticists' Manifesto" adopted at the Seventh International Congress of Genetics, held at Edinburgh in 1939. Published in *The Journal of Heredity*, September, 1939. Reprints distributed by American Genetics Association (*19*).

ences under ethics in its indices. It is true that professional codes at best can only express an ideal; their acceptance and application will depend upon the individual scientists. We believe, however, that the scientist's position in the world today makes it extremely important that his time-proved traditions be reconsidered in terms of modern circumstances and possibly written into a formal code. We believe that such an action would maintain the advance of science, increase its public support, and improve the professional relations of scientists. Improved professional relations would better morale and increase productivity among research men. Mills (*10*) has pointed out the social implications of ethical behavior in the distribution of research grants.

The planning of an ethical code for scientists should take into account first the scientist's general obligations as a member of society, and beyond that his special obligation as a scientist to protect society—here, there are many problems related to warfare, to the health and general well-being of mankind, and to nationalism versus internationalism. Such a code should preserve the scientist's ethical traditions and incorporate the scientific method. It should state the scientist's obligation to explain the nature and purposes of science, and the policies in dealing directly with the public. It should clarify the scientist's attitudes toward patents and secrecy restrictions. It should affirm the scientist's obligations to individuals—to his employer, his associates, other scientists, and his assistants and graduates—and scientists' obligation as a group to other professions.

We have merely indicated the scope of the problem. To deal with it fully in all its phases would require the efforts of scientists in many different fields of study and kinds of employment. Some of these phases have already received considerable attention. Because the results of atomic research have such unmistakable implications for society, attention has been paid to the scientist's attitude on the use of his discoveries, particularly for military purposes, and to the necessity of his being socially conscious (*3, 4, 5, 8, 10, 13*). Other phases of the problem have received little or no public consideration.

Many of the scientist's obligations are reciprocal in the sense that the scientist has grown to expect certain conditions for his work, and to a considerable extent these conditions affect the quality of his work. Sometimes his obligations are conflicting. He may at times be faced with the dilemma of obligations to his employer that conflict with obligations to the public as a whole. What should his attitude be when his employer's immediate interest causes harm to the general public? Suppose that his employer is a company that is pouring waste products into a stream and he knows that at a reasonable cost this pollution could be greatly minimized. Should he assume, as a lawyer does, that his primary obligation is to his client, and become an automatic defender of the company's position? Or should he consider that he has duties to society greater than those to the company?

A group of very pressing problems is presented in the application of traditions related to the authorship and publication of scientific researches. In the early days of science most articles carried the name of only one worker, whereas multiple authorship is now most common and sometimes ten or more persons may be involved. As a detailed example of the need for a code of professional ethics, we will discuss some of the problems involved in authorship.

General Obligations of Authors

Quality of Papers. Everyone will agree that scientific articles should be of good quality, should be original in content, and should describe all work in a reproducible fashion. These are fundamental requirements of the scientific method and yet most scientists would admit that many research articles are published that are deficient in some or all of these respects.

Claude Bernard (*2*) has described the importance of adequate details:

> In scientific investigation, minutiae of method are of the highest importance. The happy choice of an animal, an instrument constructed in some special way, one reagent used instead of another, may often suffice to solve the most abstract and lofty questions . . . . the greatest scientific truths are rooted in details of experimental investigation which form, as it were, the soil in which these truths develop.

Even casual inspection will show that many articles are not written so that the work can be repeated. Traditional procedure is often ignored in reporting new compounds; occasional articles will not give analyses of new compounds or the compounds will be poorly described so that their identity is questionable. Scientific journals lack space to print all the good material they receive today, and understandably urge authors to shorten their articles, but great care is needed to avoid eliminating important details.

Direct responsibility to prior work. The traditions of science demand that any report of scientific work must consider prior work, integrate it in the general subject, and cite proper references to it. Frequent violations of this principle must be familiar to all scientists. One of us has previously called attention to an instance of this type, particularly in relation to the naming of methods (*11*).

The basic concept behind this principle, even more fundamental than professional courtesy, is that fre-

quently the solution to a problem may already be in the literature and needless repetition is economic waste. Thorough literature searching can be defended from an economic standpoint alone. In order to speed the incorporation of new work into the general body of basic knowledge, each author has the responsibility of assisting in the integration of his work with that of previous workers.

To many scientists, establishment of priority for new discoveries is important, and organizations that seek patent protection for their work may set up involved and expensive procedures to establish the date of discovery. Is this a tradition that should be continued? Some scientific journals do not carry the date a manuscript was submitted, and few indicate whether essential changes of content have been made after that date. "Letters to the Editor" may require careful controls to prevent abuses.

Criticism and disagreement. The scientific method requires that all research work be open to critical examination and testing by researchers in the field. It also requires that dissenting theories and results be treated with tolerance, and not suppressed merely because they disagree with currently accepted ideas. Many scientists would add that mistakes and errors should be publicly acknowledged.

The widespread violation of these principles today is affecting not only the progress of science but our economy as well. Many commercial research organizations keep closed files of their researches as a matter of policy, in the belief that they will have an advantage over their competitors. Most of them do not realize that lack of criticism of the worker by qualified colleagues in his own field fosters the carrying out and perpetuation of poor or erroneous work, the continued employment and promotion of unqualified workers, and the perpetuation of poor research policies. Criticism by members of the worker's organization and by consultants is usually inadequate because of the influence of personal motives and lack of knowledge in the specific field. Objections to excessive secrecy in military research should take into account this principle as a primary consideration.

Classical examples of the value of scientific controversy are well known. When properly conducted, such debates lead to clarification and advancement of knowledge. But improperly conducted, they lead to enduring feuds, and because of this possibility, there is a tendency among editors of journals to suppress scientific polemics. A continuation or extension of this trend will be a severe blow to the scientific method. However, as stated by Wise (*13*)

> the research worker should not permit himself to become embittered or involved in useless polemics. . . . It simply means that his criticisms must be objective and that they must not descend to the plane of personalities. He must show that he is dealing with a set of data, not with an enemy.

Property rights of the scientist in his work. A currently controversial problem of the application of scientific tradition involves the rights of a researcher to his work. The decision to try to publish or reveal his research once was the sole right of the scientist. Now, with the investigator receiving financial support from others in most cases, the final decision is tending to fall on the provider of the funds. In the extreme case, what is there to prevent someone in authority from taking over the work of an associate and passing it off as his own work? What should an editor of a scientific journal do if he receives for publication a suitable manuscript from an established worker and simultaneously a letter from the supporting group saying that it should not be published? Should the supporting group be required to provide satisfactory and convincing grounds? By tradition and perhaps even by legal mandate, the rights of an artist to certain phases of the disposition of his work have been affirmed. Should these not apply equally to the scientist, whose application of his science is often an art?

At least one established graduate institution has the policy that all doctoral theses are published solely in the names of the individual graduate students. In certain instances, the idea was suggested by a member of the faculty, who carried out some preliminary work, supervised the principal research, drew or helped draw the conclusions, rewrote the thesis and wrote the final published version. Is this an example of acceptable ethics?

Publicity. Some scientists violently oppose general publicity and popularization of their work. Others seek publicity, and some even condone or support erroneous and misleading publicity. What should be the attitude of the scientist? Does he owe the public a duty to attempt to explain the purpose and significance of his work? Should chicanery and excessive or misleading publicity on the part of scientists and nonscientists be exposed as a function of scientific societies? It is of interest that the *Principles of Medical Ethics* includes a considerable discussion of the impropriety of advertising and publicity-seeking and that AMA members are required to advise the public against misrepresentation. A firm stand on this issue by scientists generally might be of considerable help in establishing the professional status of the scientist in the public mind.

Multiple Authorship

With the change in status of research, owing to its being produced not by independent individuals but by

several dependent workers or even large groups, the scientific tradition in respect to the etiquette of authorship needs reinterpretation or extension. The responsibilities involved in multiple authorship or group research must be analyzed.

"Senior" authorship and order of names. To many scientists, the order of the authors' names on a publication has a significance. Is this a tradition that should be preserved, clarified, and enforced, or is it an outmoded, unessential form of etiquette? In current publications, the application seems uncertain and haphazard. Should the concept of the "senior author" (the first one listed) be preserved? If so, should the senior author be the person highest in the administrative rank, the one who has done most of the laboratory work, the one who has written the paper, the one who furnished the original idea, or the one whose technical skill and thoughts have carried along the research?

Administrators and financial supporters. In publications, what consideration should be given to administrators and financial supporters? Some scientists might say that they should be indicated as authors only when their contribution to the actual solution of the problem has been substantial, continuous, and of a high level. Probably most scientists would agree that mere general administrative supervision of a project or even the suggestion of the original idea for the project is insufficient for an authorship. Certainly no one should be granted authorship of any type merely because he has seniority or is in charge of a laboratory. We cite as an example a man serving as technical liaison between a company and a research organization who insisted that his name be included as an author, before he would ask for supporting funds for the research, although his total contribution was limited to this action.

Graduate students and technical assistants. Criteria are necessary for assessing the role of graduate students and technical assistants in relation to authorship. Should not senior authorship for a graduate student be limited to those instances in which a real contribution, beyond adequate laboratory work, has been made? On the other hand, is it not the duty of the directing professor to encourage the student to his maximum performance, rather than use him as a laboratory assistant? If a technical assistant is to be given authorship of any type, more than an adequate performance of routine methods should be required of him.

Group projects. An example of the large group projects that characterize modern science is the penicillin research during World War II. Industrial organizations provide many more examples. Frequently there is no attempt on the part of administrators to set up the program so that the work of individual investigators is kept discrete. The improved quality of work resulting from the establishment of definite responsibility might be the basis for making a definite statement in regard to this problem. The interpretation of the scientific tradition in terms of modern group research is an extremely important and as yet unexplored field.

Preparation of manuscripts. The published paper is the final record of the finished research work, and the medium through which the information is made generally available and useful. With the present shortage of publication space, the preparation of the manuscript becomes more important than ever. Rigid adherence to established scientific traditions on the part of authors and editors becomes increasingly essential.

To many persons, the preparation of a research paper may seem to be a routine matter, but actually it requires a high order of skill and technical knowledge and an acquaintance with scientific traditions. In many researches the actual preparation of the manuscript, the integration of the findings with the prior related work, consideration of the significance of the data, and arrangements for publication may require a considerable portion of the time and skill required for the entire project. Possibly the actual preparation of the manuscript should be a factor in defining the responsibilities of the senior author. Laboratory workers without a good background of knowledge, and research administrators without close daily contact with the laboratory work and a thorough knowledge of the field probably should be discouraged from actual preparation of the manuscript. On the other hand, simple manuscript revision, in spite of the poor writing ability of many scientists, should not generally be made the basis for authorship of a research paper. Still another problem is determining the duties and responsibilities of the referees of scientific articles.

The interpretation of scientific traditions, and their formal codification, if that is to be accomplished, are essentially a task for scientists. As this discussion demonstrates, the problems of interpretation are manifold and if they are not solved they may severely hinder the progress of science. The harm done may not only be general but may apply particularly to industrial research of the group type. Incidental effects of the code, but of considerable importance, would be the great improvement in morale among scientific workers, the improvement in the quality of scientific work, the assistance it would give to editors of scientific journals and research administrators, and the basis it would provide for exposing poor work and even instances of chicanery. It would be of great

assistance in the training of graduate students in the scientific method. The preparation of a formal code of professional ethics should be of considerable value in establishing the professional status of the scientist in the public mind. It seems more than a coincidence that the groups that already have formal statements of their social and professional responsibilities and have definite rules of professional behavior are those definitely accepted by the public as having professional status.

As we have pointed out, violations of professional ethics on the part of scientists are frequent and familiar to all scientists. Sometimes they are deliberate violations for personal power or gain. Frequently, they are the results of carelessness or unfamiliarity of research administrators or research workers with the established traditions. They may even result from excessive pressure of work, a condition that appears common in industrial research. Some violations are the result of misguided attempts by editors and reviewers of scientific journals to shorten articles.

Is not the time opportune for our scientific organizations, or some agency of Unesco, to consider the manner of the application of scientific traditions to the newly developed conditions of scientific research? We suggest that the establishment of a definite code of professional ethics and conduct by our major scientific groups would have profound and favorable effects for science, society, and the scientist.

A mere statement of principles would be of help. An extensive codification and attempt to discipline or expose gross violations might be desirable. Our societies have various ways and means of enforcing regulations. Exclusion from membership and control of publications and means of publicity are powers that could be used to control unscrupulous and continuous violations. There may appear to be an anomaly in scientists' establishing a formal code of ethics to preserve traditions that include independence in their work, but this merely reflects an anomaly in present conditions of scientific work. It seems far better for scientists to affirm such a code positively than to be regimented to an increasing extent without any control over the conditions under which they must work. A. V. Hill (*8*) puts the problem as follows:

> The important thing is not a creed "which except a man believe faithfully he cannot be saved." What matters is that scientific men should argue and discuss the matter of scientific ethics as one of infinite importance to themselves and the rest of mankind with the same honesty, humility and resolute regard for the facts they show in their scientific work.
>
> If they do, then something will surely crystallize out from their discussion, and I have faith enough in the goodness and wisdom of most scientific men to believe that the result on the whole will be good and wise. It may in the end be embodied in a new Hippocratic Oath; or it may be absorbed in trade union rules for the scientific profession; or ethical behavior in science may just come to be accepted as an honorable obligation as unbreakable as that of accuracy and integrity.

We add that all problems will not be solved, but science is expanding and moving. The rate of progress will be profoundly affected by the consideration that is given to the maintenance and proper application of time-proved scientific traditions as the conditions of scientific work change.

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Catalysis and Carbonium Ions in Petroleum Formation

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IN THREE RECENT PAPERS (*4, 5, 6*) some evidence was presented that active surface minerals, in the strata in contact with petroleums, or the heavy bitumen that preceded typical petroleum, played an essential role in the formation of petroleums. It was suggested that such minerals have acted as catalysts and that the many hydrocarbons now found in petroleum were formed by chemical reactions through a carbonium ion mechanism. Two recent papers (*9, 15*) have brought forward experimental evidence that in industrial catalytic cracking with certain types of catalysts the reactions that take place involve a carbonium ion mechanism. There is much evidence that the two sets of phenomena are related. All of the evidence cannot be reviewed here but the more important considerations are:

(1) Petroleums appear to have been formed from original organic source material laid down in marine sediments, changing slowly through heavy bitumens progressively with age and depth (*2, 5*) to petroleums containing light and heavy oils, except in certain unusual circumstances (see par. 5).

(2) Both the geological (*10*) and chemical (*3*) facts are conclusive as proving a low temperature history, in most cases not exceeding about 140° F.

(3) Calculations from the known rates of cracking at 750° F, or higher, indicate that at the temperatures in oil reservoir rocks substantially no change in hydrocarbon oils could have been effected by *heat alone* during elapsed geologic time (*13*) even to the Ordovician, and most of our American petroleums are not older than Cretaceous.

(4) Sedimentary rocks, shales, and sands, having marked catalytic activity, as measured by the polymerization of unsaturated hydrocarbons, are much more common and widely distributed than was formerly supposed. This activity is not limited to special clays of the type of fuller's earth (*4*).

(5) Heavy petroleums are known that contain little or no light oils and are old enough (Cretaceous or older) to have been converted to an average petroleum containing 25 to 30 percent gasoline. Such heavy oils occur usually in limestone reservoir rocks which have no catalytic activity, as for example the heavy Panuco oil of Mexico found in a Cretaceous limestone, a heavy crude devoid of gasoline found in the Arbuckle limestone (Ordovician) in northern Oklahoma and Kansas, and heavy black oils produced from limestone in Wyoming. In other cases, relatively light crudes may have been formed before migrating into a limestone reservoir. It has recently been found (*5*) that the tar sand in Athabasca, which is Cretaceous, is a clean quartz sand free from clay or fines and is noncatalytic, as tested for polymerizing activity (see following discussion of catalyst activity). Since this sand is not consolidated or lithified the tar probably impregnated the sand early in its history.

(6) The percentages of individual hydrocarbons in petroleums bear no consistent relation, even in the case of a single petroleum, to any calculated equilibrium mixture or ratios, for any particular temperature. If temperature alone were the controlling factor then all oils of substantially the same age and temperature history should be substantially the same and individual hydrocarbons, as for example the isomeric hexanes, should be found in the same relative proportions. This is not even approximately true.

(7) Crude petroleums of widely different composition are known that occur in strata separated vertically by only a hundred feet or so, with no unconformity between them, and whose age and temperature histories are thus substantially the same. Such differences, heretofore very puzzling, are readily accounted for by wide differences in catalytic activity of the rocks with which they are in contact.

(8) The percentages of cyclopentanes and cyclohexanes in all gasolines that have been investigated cannot possibly be accounted for by thermal degradation of any marine source material containing such C_5 and C_6 rings (*6*). Substances containing cyclopentane rings are exceedingly rare in nature. High yields of a trimethyl cyclopentane have been formed from isobutene under polymerizing conditions.

(9) A study of the catalytic action of fuller's earth and several synthetic alumina-silica catalysts on propylene, at 350° C, below common cracking temperatures, showed that isoparaffins and olefins of C_5, C_6, C_7, C_8, and C_9 and higher molecular weight hydrocarbons were formed (*8*). This showed that paraffin syntheses, hydrogenation, and carbon chain splitting occurred. The results obtained in this investigation, as well as the products obtained by commercial catalytic cracking, varied with the nature of the catalyst.

The essential problem in explaining petroleum formation is to discover a plausible chemical mechanism

to account for the formation of the great diversity of hydrocarbons, including normal paraffins and branched chain paraffins, cycloparaffins and alkylated cycloparaffins and aromatics. If, instead of such complex mixtures, petroleums consisted of only a few hydrocarbons, as in the natural occurrences of normal paraffins in plants where the paraffins are associated with fatty acids having one more carbon atom than the paraffins, then it would be obvious or strongly indicated that the hydrocarbons were simply derived from fatty acids by loss of CO_2. However, the characteristic complexity of petroleums is strikingly analogous to the results obtained by Gayer and the results of low temperature catalytic alkylations of isoparaffins and olefins now generally believed to take place through a carbonium ion mechanism.

The choice of mechanisms that might account for such complex hydrocarbon mixtures as petroleums appears to be limited to two: free radicals and carbonium ions.

It should be kept in mind that any hypothetical mechanism should be operable within the natural and common conditions of petroleum formation, i.e., temperatures usually not exceeding about 140° F and exceptionally as high as 225° F and as low as 100° F, and contact through millions of years with certain mineral formations.

It is true that there are many chemical reactions that take place at or slightly above room temperature, and that are believed to involve a free radical mechanism. However, as shown by the work of Morris Kharasch, such reactions are catalyzed by such substances as unstable organic peroxides, or by short wavelengths of light, both of which agents are believed to form free radicals. Both catalysts are patently excluded by the environment, in deeply buried strata, in which petroleum has been formed. The other common condition for producing free radicals is thermal decomposition at temperatures much higher than can be considered in this problem.

Reactions of hydrocarbons involving a carbonium ion mechanism are not necessarily conditioned upon high temperatures, for many of them take place at low temperatures—as, for example, in alkylation processes where refrigeration is required to maintain temperatures below about 60° F. In a paper published in 1948 (*4*) it was stated:

> It is now generally accepted that all of these alkylation results are best explained by the formation of carbonium ions. The low temperature formation of the great number of hydrocarbons found in petroleum through the action of active-surface minerals must have a similar chemical mechanism. Further evidence that the catalytic active-surface minerals play an important role in the formation of petroleum is found in the nature of the hydrocarbon constituents of typical petroleums. The fact that straight-run gasolines and kerosenes contain no unsaturated or olefinic hydrocarbons is a strong indication of this. Also the complexity of such oils or, in other words, the very large number of hydrocarbons, isomeric paraffins, naphthenes and aromatic hydrocarbons, has no other plausible explanation.

B. S. Greensfelder (*9*) and his co-workers, in their study of the mechanism of catalytic cracking, state:

> The properties of carbonium ions, which are postulated to represent the reactive form of the hydrocarbon in conventional catalytic cracking, also determine the mechanism of reaction and the type of product in many other acid-catalyzed hydrocarbon reactions such as isomerization, polymerization, paraffin alkylation and hydrogen transfer reactions of olefins, also the isomerization of paraffins and the alkylation of aromatics.

In their study, likewise in the work of C. A. Thomas, good qualitative correspondence between acidity (pH and reaction of the dry solid with ammonia) and catalytic activity is established. They state that the carbonium ion mechanism of catalytic cracking is

> . . . directly coupled with the requirement that the acidic oxide type of cracking catalyst must make available reactive positive hydrogen ions (protons) capable of producing carbonium ions . . .

on contact with the oil. Definite experimental evidence was obtained for the strongly acidic character of silica-alumina, silica-zirconia-alumina (U.O.P. Type B) and acid-treated clay catalysts. These catalysts at ordinary temperatures are also good polymerization catalysts.

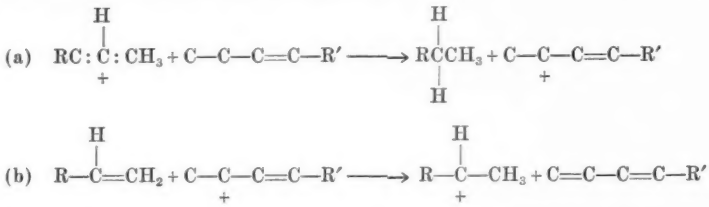
A study has recently been made of the acid strength of surfaces by the adsorption of various indicators (*16*). The substances investigated included silica-alumina, the silica-alumina bead catalyst used in catalytic cracking by the Socony-Vacuum Company, a synthetic silica-magnesium catalyst, alumina, and silica gel. It was concluded that pure silica gel has a very low acidity but the surface acid strength of the silica-alumina and silica-magnesia, between that of 0.1 and 1.0 *N* HCl, is an intrinsic property of these materials. The author, C. Walling, states:

> It emphasizes the possibility that many examples of heterogeneous catalysis are, fundamentally, cases of acid catalysis occurring on an acid surface . . . for which there appears to be considerable support in the literature.

He points out that activated clays are effective catalysts for acylation and alkylation of aromatic hydrocarbons (*12*), and polymerization of olefins.

According to C. A. Thomas (*15*) olefinic hydrocarbons are converted to paraffins without any external source of hydrogen. This hydrogen is supplied by

converting part of the olefinic hydrocarbons into hydrocarbons having less hydrogen, and may be represented by the carbonium ion mechanism in two steps,



Thus two olefin molecules can be converted into a paraffin and a diolefin and

By repeating the same type of process, the diolefin may be converted to a triolefin and on to an aromatic hydrocarbon.

The formation of the aromatic hydrocarbons found in petroleum oils has always been difficult to account for by purely thermal means in view of the fact that A. W. Francis (*7*) and others (*14*) have stated on thermodynamic grounds that aromatic hydrocarbons cannot be formed from paraffins with splitting off of hydrogen under about 500° C, a temperature far outside the possibilities in petroleum formation. The formation of aromatic hydrocarbons from unsaturated hydrocarbons by hydrogen disproportionation by the action of catalysts such as fuller's earth has long been known, as for example the conversion of certain terpenes to *p*-cymene and *p*-menthane. This is an instance of the type of reaction involving a carbonium ion mechanism discussed by Thomas.

It was also suggested by Thomas that the presence of a small amount of an olefin may be necessary to start the carbonium ion chain reactions, and at high temperatures, as in commercial catalytic cracking reactions, the olefins believed to be necessary are formed by thermal decomposition, and then

. . . the carbonium ions produced continue the reaction chainwise via the hydride ion exchange mechanism proposed by Bartlett [*1*] for the alkylation of olefins with paraffins.

However, it has been shown (*11*) that in the isomerization of butane, which is also believed to occur through a carbonium ion mechanism, 0.01 percent of butenes suffices to initiate the reaction. It is uncertain whether or not the lower boiling fractions of petroleum oils now contain olefinic hydrocarbons in any such proportions, but any conceivable organic source material for petroleum must have contained unsaturated fatty acids or their polymers. Petroleum in transition stages must have contained more than sufficient olefinic substances to initiate such carbonium ion reactions if the butane isomerization reaction is any indication of the proportions necessary.

It may be supposed that a mechanism of petroleum formation involving carbonium ion reactions would require the presence, somewhere in the strata, of carbonized residues such as are formed in commercial catalytic cracking processes, but the presence of substantial percentages of aromatic hydrocarbons, which have been otherwise difficult to account for, is one very good answer. Also highly unsaturated hydrocarbons are readily polymerized, as mentioned in the summary in the first part of this paper. Most petroleums contain heavy residues having high carbon-hydrogen ratios which have never been satisfactorily characterized. Oils free from heavy residues and having very high percentages of gasoline are generally believed to have been the result of partial purification by adsorption during migration.

It is submitted that hydrocarbon reactions involving carbonium ions and initiated by the catalytic action of acid silicate minerals, particularly clays, explain satisfactorily many of the problems of petroleum formation hitherto not understood.

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Technical Papers

Houseflies Resistant to Benzene Hexachloride

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In October 1948 the junior author, a staff member of the International Health Division of The Rockefeller Foundation, working in cooperation with the Egyptian Ministry of Health, initiated a housefly control campaign in the Egyptian village of Quaranfil. One of the measures used was the application of benzene hexachloride dusts containing 2.4% of the gamma isomer to all places suspected of being breeding areas. The treatment was renewed whenever it showed signs of losing its effectiveness. During the first 10 months fresh applications were made approximately once a month. A great reduction of houseflies was maintained throughout most of this period. In August, September, and October of 1949 the intervals between dustings were gradually shortened until applications were being made weekly because an adequate control could no longer be maintained. It was suspected that a strain of houseflies had developed that was resistant to benzene hexachloride.

To find out if this suspicion was correct a series of laboratory tests was run by the senior author during November and December, 1949, against houseflies (*Musca domestica vicina* Macq) collected from nine different sources, including six villages in addition to Quaranfil, a slaughterhouse in one of the suburbs of Cairo, and a laboratory-reared colony. Quaranfil was the only place in which large scale housefly control measures were being used.

The tests were run on plywood panels (1 ft square) that had been sprayed with an acetone solution containing 1.25% benzene hexachloride. The sprays were prepared from a technical grade product having a 20% gamma isomer content. Solution was applied, 10 ml to each panel, to obtain a dosage rate of 25 mg of the gamma isomer per square foot. Within one week after treatment adult houseflies were exposed on these treated surfaces for varying periods of time, confined under half-sections of Petri dishes. A previously unused surface area was used each time. After exposure the flies were transferred to untreated screen cages, furnished honey and water, and held for 24 hr, at which time mortality counts were made. The results listed in the tables are averages of six tests; three were run on each of 2 days.

In one series all nine colonies were exposed for 30 min. As shown in Table 1, at least 99% mortality was obtained within 24 hr against the eight colonies that had not been subjected to control measures. In contrast, less than half of the Quaranfil strain was killed, indicating that this strain actually had acquired considerable resistance to benzene hexachloride.

Another series was run with the Quaranfil, slaughterhouse, and laboratory strains, to obtain more precise information on the degree of resistance that had developed. In these tests the exposure period was varied between 5 min and 120 min to obtain a range of mortalities that would permit a comparison of the contact times required to kill similar percentages of the different colonies. In all, 1,796 male and 1,511 female flies were used in these tests.

TABLE 1

TOXICITY OF RESIDUAL DEPOSITS OF BENZENE HEXACHLORIDE TO NINE HOUSEFLY STRAINS

Colony	No. of insects used		Percent kill in 24 hr	
	Male	Female	Male	Female
Kafr Aho Gomma ..	123	51	100	100
Balaks	118	76	100	100
Dandana	64	105	100	100
Kam Asfar	93	86	100	100
Z. Naggar	133	38	100	100
Sandyong	123	81	100	100
Slaughterhouse	119	92	100	99
Laboratory	192	38	100	100
Quaranfil	58	150	48	12

The results obtained in the second series are listed in Table 2. It is readily apparent that the Quaranfil strain was much more difficult to kill than the slaughterhouse or laboratory strains. An exposure that was sufficient to cause 100% mortality of those from the two untreated sources killed only 15% of the males and 12% of the females from the resistant stock. The 5-min exposure killed 65%–67% of the slaughterhouse and laboratory females but a 2-hr exposure was required to kill a comparable percentage of those from the village where benzene hexachloride treatment had been given, indicating the Quaranfil flies were about 24 times as resistant to this insecticide as the other two strains. The degree of resistance acquired by the males appeared to be even greater.

With female flies the greatest differences were observed in the 30-min tests, where the mortality obtained in individual tests was always at least 67% lower for the resistant flies than the corresponding exposure of slaughterhouse or laboratory flies. Similarly, the kill of males from the untreated sources always exceeded that of the Quaranfil stock by at least 78% in the 5-min tests.

[1] On assignment from Bureau of Entomology and Plant Quarantine, USDA, Orlando, Florida, to the U. S. Naval Medical Research Unit No. 3, Cairo, Egypt.

[2] The International Health Division of the Rockefeller Foundation, Cairo, Egypt.

TABLE 2

RELATIVE SUSCEPTIBILITY OF THREE HOUSEFLY STRAINS TO RESIDUAL DEPOSITS OF BENZENE HEXACHLORIDE

Housefly strain	No. of insects used		Percent kill in 24 hr	
	Male	Female	Male	Female
		5-min exposure		
Slaughterhouse	97	166	100	65
Laboratory	147	146	100	67
Quaranfil	71	96	6	4
		10-min exposure		
Slaughterhouse	93	133	95	90
Laboratory	207	101	99	74
Quaranfil	108	122	8	4
		30-min exposure		
Slaughterhouse	119	135	100	100
Laboratory	221	102	100	100
Quaranfil	110	105	15	12
		60-min exposure		
Slaughterhouse	136	93	100	100
Laboratory	199	88	100	100
Quaranfil	125	116	84	42
		120-min exposure		
Slaughterhouse	...	...	...	...
Laboratory	...	...	...	...
Quaranfil	163	108	86	62

There were no reversals in any of the comparisons.

Entomologists have hoped that benzene hexachloride would be one of the residual-type insecticides that could be used satisfactorily in situations where houseflies have developed resistance to DDT. The results obtained in Quaranfil indicate that any benefit derived from a change to this insecticide might be only temporary.

Acceleration of Carbon Monoxide Elimination in Man by High Pressure Oxygen[1]

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Claude Bernard (*2*) was the first to point out that carbon monoxide produces hypoxia through its reversible combination with blood to form carboxyhemoglobin, and pure oxygen at normal barometric pressures has been used as an effective therapeutic aid in the treatment of CO poisoning ever since it was first tried by Linas and Limousin (*8*). The relative affinity relationship between CO and O_2 for hemoglobin has been enunciated by Douglas, Haldane, and Haldane (*5*) in the form $\frac{[COHb]}{[HbO_2]} = K\frac{[pCO]}{[pO_2]}$ where K, the relative affinity constant, has been measured to be 210 for man (*12*). The rationale for increasing the partial pressure of inspired O_2 in the treatment of CO poisoning, therefore, seems clear on the basis of mass action consideration alone, and a direct relationship between alveolar pO_2 and the rate of CO elimination from the body might be expected. Such a relationship has been demonstrated recently for man (*10*), and will be reported in detail later. The rate of CO elimination in man is increased approximately fivefold from a half-time of over 4 hr while breathing air to a half-time of about 45 min while breathing pure oxygen, corresponding to the fivefold increase in pO_2.

The most serious effect of CO inhalation was convincingly demonstrated by Haldane (*7*) to be the combination of the gas with the blood hemoglobin and the consequent reduction in O_2-carrying capacity of the blood. In his classic experiment, a mouse was exposed in a pressure chamber to one atmosphere of CO and two atmospheres of oxygen with no loss of consciousness or obvious ill effects, the mouse apparently having met its metabolic oxygen requirement by utilizing the greatly increased oxygen in physical solution in the blood plasma. There is implicit in this experiment the use of oxygen at pressures higher than normal barometric pressure for the treatment of CO poisoning, and End and Long (*6*) have shown the worth of high pressure oxygen in treating laboratory animals after exposure to CO. Reluctance to use high pressure oxygen in the treatment of persons suffering CO poisoning stems from the toxic nature of oxygen itself at pressures of one atmosphere and higher; however, as pointed out by Bean (*1*), there is a relationship between time and concentration in the development of oxygen poisoning. This makes it possible to select an optimal combination of exposure time and ambient oxygen partial pressure such that the rate of CO elimination may be materially increased without incurring the risk of oxygen poisoning.

Following mild, acute exposure to CO, ten volunteer subjects, comprising five men and five women, were placed in a recompression chamber[2] at 22 psi gage pressure. Measurements of the rate of CO elimination were carried out while the individuals seated at rest, breathed pure oxygen for 1 hr. In this way, the subjects were exposed to an ambient pO_2 of 2.5 atmospheres. The procedure consisted in allowing the subject to rebreathe a mixture of 250 ml of CO and 2 l of air from a rubber bag for 30 sec. The individual was then seated in the recompression chamber, and the ambient pressure was raised to 2.5 atm, absolute. Oxygen breathing was begun through an A-14 mask with free flow from a tank of medical oxygen, and the first blood sample was withdrawn from the antecubital vein after a few minutes. The initial blood levels of CO ranged from 20% to 30% COHb, and blood samples were withdrawn by venepuncture every 15 min during the hour of oxygen breathing. The samples were analyzed for CO content by the method of Scholander and Roughton (*11*), and the rate of elimination was determined as the slope of the line of least squares through a plot of the logarithm of blood concentration against time. As shown elsewhere (*10*), CO elim-

[1] The authors wish to express thanks to the Office of Naval Research for making this work possible under Contract N7 onr-295, Task Order IV, Project No. NR 122-307.

[2] Thanks are due to the Commandant, San Francisco Naval Shipyard and to Lieutenant W. M. Minor, U. S. N., and the men of the Ship Salvage Unit for permission to use the recompression chamber and for its operation.

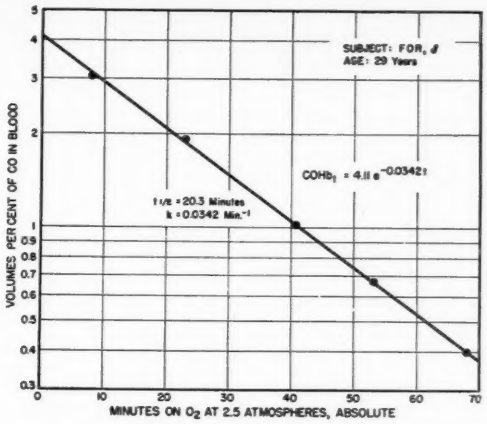
SUBJECT: FOR, ♂
AGE: 29 Years
COHb$_t$ = 4.11 e$^{-0.0342t}$
t1/2 = 20.3 Minutes
k = 0.0342 Min.$^{-1}$
VOLUMES PER CENT OF CO IN BLOOD
MINUTES ON O2 AT 2.5 ATMOSPHERES, ABSOLUTE

FIG. 1. CO elimination curve from the venous blood of a man breathing pure oxygen at an ambient pressure of 2.5 atm, absolute, following mild, acute exposure to CO. The line and equation parameters were obtained by the method of least squares. Each point is the mean of a triplicate blood analysis.

ination under standard conditions of activity follows a simple exponential rate expression of the type: $COHb_t = COHb_0 e^{-kt}$ where $COHb_t$ is the blood concentration of CO at time t, $COHb_0$ is the concentration at zero time, and k is the rate constant measured as the slope of the line described previously. The rate constant, k, represents the fraction of blood CO eliminated per unit time, and may be expressed as a half-time of elimination by the relationship: $t_{\frac{1}{2}} = \frac{\ln 2}{k}$. The results of a typical experiment are shown in Fig. 1, and it is to be noted that the slope of the time, i.e., the rate constant, is determined on the basis of five points, each of which is the mean of a triplicate analysis on the blood samples they represent.

The CO elimination rate data obtained on the ten subjects are seen in Table 1. Care was taken to select individuals in a comparable age group so as to control the effect of age on CO elimination (*9*).

TABLE 1

RATE OF CO ELIMINATION BY MEN AND WOMEN BREATHING PURE OXYGEN AT 2.5 ATMOSPHERES, ABSOLUTE

Male subjects	Age (yr)	k (min^{-1})	$t_{1/2}$ (min)	Female subjects	Age (yr)	k (min^{-1})	$t_{1/2}$ (min)
STR	34	0.0363	19.1	WAL	25	0.0447	15.5
GLA	24	0.0262	26.5	JOH	28	0.0465	14.9
KAW	30	0.0318	21.8	THI	27	0.0444	15.6
PAC	33	0.0289	24.0	POW	27	0.0495	14.0
FOR	29	0.0342	20.3	SYR	27	0.0447	15.5
Mean	30.0	0.0315	22.3	Mean	26.8	0.0460	15.1

As discussed elsewhere (*10*), a significant sex difference in the rate of CO elimination is apparent in these data. It may also be noted that the half-time of elimination is of the order of 20 min, so that 1 hr of oxygen breathing in the recompression chamber at 2.5 atm, absolute, will result in reduction of blood carboxyhemoglobin level to 10% or 15% of whatever the starting level might have been. It follows, then, that 1 hr is the maximum exposure to a pO_2 of 2.5 atm necessary for lowering blood CO to safe limits, i.e., below three volumes percent. One hour is a completely tolerable exposure to this pO_2 in regard to oxygen-poisoning symptoms (*1*).

For purposes of comparison, mean rates of CO elimination by men and women breathing ordinary air and pure oxygen at normal barometric pressure are given in Table 2. The alveolar pO_2, as calculated from the equation of Brink (*3*), is included because blood is in equilibrium with alveolar rather than ambient pO_2, and hence the alveolar pO_2 is more meaningful in considering relative O_2 and CO affinities for hemoglobin.

Again, the pronounced sex difference is seen in the rate of elimination, women losing CO about 30% more rapidly than do men under comparable conditions; for present purposes it suffices merely to point out this finding. It may also be seen from Table 2 that although there is a great increase in CO elimination rate when pure oxygen is breathed at normal barometric pressure, the half-time of elimination is still long in terms of the rapidity with which the deleterious effects of hypoxia set in. Hence, in treatment of CO poisoning, where not only resuscitation of the victim but avoidance of serious and permanent after effects of prolonged hypoxia is also important, the further increase in CO elimination rate by administration of O_2 under high pressure seems of considerable practical value.

TABLE 2

COMPARISON OF MEAN RATE OF CO ELIMINATION BY MEN AND WOMEN BREATHING OXYGEN AT VARIOUS PARTIAL PRESSURES

Ambient pO_2 (atm)	Calculated alveolar pO_2	Male				Female			
		No. of subjects	Mean age (yr)	Mean k (min^{-1})	Mean $t_{1/2}$ (min)	No. of subjects	Mean age (yr)	Mean k (min^{-1})	Mean $t_{1/2}$ (min)
0.2	0.14	5	30.0	0.0028	249	5	26.2	0.0039	179
1.0	0.89	10	27.1	0.0150	47	5	26.6	0.0199	36
2.5	2.37	5	30.0	0.0315	22	5	26.8	0.0460	15

Another point to consider is the increase in oxygen carried in physical solution by the blood plasma. Under normal conditions of air breathing, the amount of dissolved oxygen is insignificant in comparison with the metabolic requirements of the body. The dissolved oxygen accounts for 1% of the normal arterial blood oxygen content, and is approximately 0.2 vol % (*13*). The arteriovenous oxygen difference for man at rest as measured between arterial blood and mixed venous blood by right auricle catheterization is found to be about 4.5 vol % (*4*). If, however, pure oxygen is breathed at 2.5 atm ambient pressure, the dissolved oxygen may be calculated to increase to just 4.5 vol %. Direct measurement of the dissolved oxygen under these conditions was not made

in the present study, but it was noted that venous blood samples withdrawn for CO analysis were consistently a bright red color in the high pressure experiments, in contrast to those drawn under other conditions, indicating a high degree of oxygen saturation of venous blood. In any case, it is apparent that the resting metabolic oxygen needs may be met almost completely by the dissolved oxygen when pure oxygen is breathed at 2.5 atm pressure. Thus, in addition to a significant acceleration in CO elimination rate, administration of oxygen at high pressure would also seem to relieve hypoxia immediately in victims of CO poisoning.

Clinical trial of high pressure oxygen as a means of therapeusis in CO poisoning therefore appears warranted, and is recommended where suitable pressure chamber facilities are available. There is no evident reason why its use cannot be coupled with a number of standard mechanical resuscitative devices, thereby extending its application to cases where respiration has stopped. In general, to go beyond CO poisoning, high pressure oxygen might be used profitably in many situations where the hemoglobin oxygen transport mechanism has been rendered inoperative, and may be regarded as a valuable adjunct to the already well-established technique of oxygen therapy.

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Further Investigation of the Reducibility of Lyophilized Catalase

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It was reported by Dounce and Howland (*1*) that crystalline beef liver catalase became completely reducible with sodium hydrosulfite after lyophilization, as shown by the change in the visible absorption spectrum, although activity of the material per dry weight was reduced only to about one-third of the value obtained before lyophilization. Keilin (*2*) subsequently denied that these experimental results had been interpreted correctly, stating that a mixture of denatured and undenatured catalase must have been obtained, in which only the undenatured catalase was active and only the denatured catalase was reducible. No experimental work was offered to support these statements, however.

Our previous work was handicapped by the lack of a modern spectrophotometer. We have recently repeated the experiments using the Beckman spectrophotometer, and have completely confirmed our previous results, as indicated by the accompanying figures.

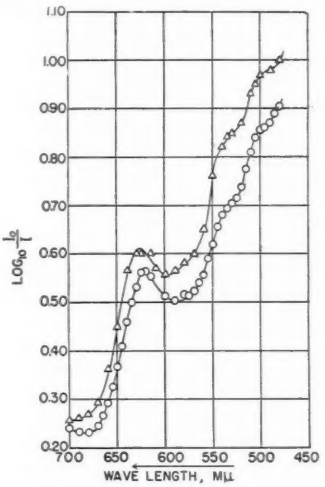

Fig. 1. Absorption spectra of lyophilized and nonlyophilized catalase. △ = 26.4 mg lyophilized catalase, Kat. f. = 14,000 in 4 ml of M/10 phosphate buffer, pH 8.0. ○ = 26.4 ml nonlyophilized catalase, Kat. f. = 25,000 in 4 ml of M/10 phosphate buffer, pH 8.0, containing 10% NaCl.

Fig. 1 shows the spectrum of a sample of recrystallized catalase which had not been lyophilized, with a Kat. f. value[1] of 25,000, together with the spectrum of a different sample of lyophilized material of Kat. f. about 14,000 which had been prepared from a sample of recrystallized catalase of Kat. f. about 23,000. The location of the three principal absorption bands is the same, but contrary to previous results (*1*) the spectra do not superimpose exactly. This might be partly ascribable to a difference in ionic strengths of the solutions, since M/10 phosphate buffer of pH 8.0 made up to contain 10% NaCl was used as the solvent for the material which

[1] The term *Kat. f.* is an abbreviation for *Katalase Fähigkeit.* It was introduced by von Euler and Josephson (*4*), and means

$$\frac{K \times \text{dilution}}{\text{g enzyme}}.$$

Here *K* is the so-called monomolecular reaction velocity constant extrapolated to zero time (*3*); *g enzyme* refers to the dry weight of enzyme per millimeter of the stock solution; and *dilution* means the number of times the stock solution is diluted before carrying out the determination.

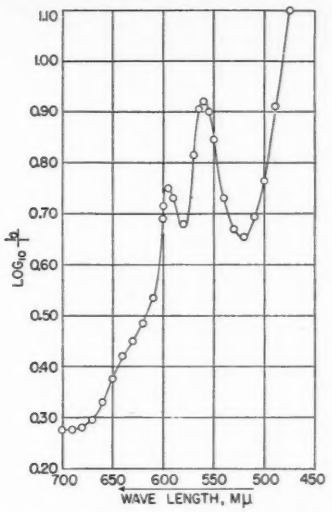

FIG. 2. Absorption spectrum of lyophilized catalase, Kat. f. = 14,000 (same sample as used for △, Fig. 1), after reduction with $Na_2S_2O_4$: 26.4 mg in 4 ml of M/10 phosphate buffer, pH 8.0.

had not been lyophilized, whereas M/10 phosphate buffer of pH 8.0 without NaCl was used as solvent for the lyophilized material. NaCl was omitted where it was not needed to dissolve the material, because it inevitably caused the gradual formation of a precipitate in the solution. Moreover, the curves were not adjusted so as to coincide at any particular point, as they were in the earlier work.

Fig. 2 shows the absorption spectrum of the lyophilized catalase sample which had been reduced with $Na_2S_2O_4$. In this case, also, the solvent was M/10 phosphate buffer of pH 8.0, without NaCl. A two-banded spectrum is obtained which is characteristic of ferroheme compounds. It seems certain that the catalase has really been reduced, since treatment of lyophilized catalase with sodium boron hydride, $NaBH_4$, gradually causes the production of a spectrum with bands at the same location as those observed with hydrosulfite reduction. Moreover, if carbon monoxide is passed into a solution of lyophilized catalase which has been reduced with hydrosulfite, the bands are shifted from 595 mμ and 560 mμ to approximately 576 mμ and 544 mμ.

It can be seen from Fig. 2 that the amount of residual unaltered catalase left over after reduction with hydrosulfite must be very low, as judged by the smallness of the bulge in the curve at about 640 mμ. In spite of this, the Kat. f. of the lyophilized material was approximately 14,000 as compared with a Kat. f. of about 23,000 before lyophilization. Thus a major portion at least of the lyophilized catalase must be active, and no more than 5%, or at most 10% of the lyophilized material can be in the form of undenatured catalase. The only way to escape the conclusion that the lyophilized, reducible catalase is active would be to assume a great enhancement in activity of the small portion of catalase that may have escaped change during lyophilization. Even if the Kat. f. of this material were doubled, the activity of the lyophilized sample could not be explained in this manner. We feel quite safe, therefore, in reiterating our original conclusion (*1*) that lyophilized beef liver catalase is changed in some way so as to render it reducible. As stated previously (*1*), completely heat-denatured catalase behaves in quite a different manner.

The most likely explanation of the behavior of lyophilized catalase reported here and previously (*1*) is that a mild sort of denaturation has loosened the attachment of the iron atom to the protein part of the molecule so that the iron becomes reducible but still remains active catalytically. A detailed investigation of this phenomenon would be worth while to someone working on the mechanism of catalase action or on the phenomenon of protein denaturation. For the benefit of any such investigator, it should be noted that the flask in which the enzyme is being lyophilized must be kept in the air during evaporation of the water and not in a cooling bath. If a cooling bath of ice and water is used, the enzyme can be lyophilized without any apparent change in its behavior.

The Kat. f. values for our recrystallized catalase samples are somewhat lower than usual but this fact does not alter the arguments presented.

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Methods of Preparing Bone and Tooth Samples for Viewing in the Electron Microscope[1]

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One of the main characteristics of bone is its resistance to bending, torsion, compression, and tensile stresses. This resistance is offered by a combination of

[1] This paper is based on work performed under contract with the United States Atomic Energy Commission at the University of Rochester Atomic Energy Project, Rochester, New York.

[2] Grateful acknowledgment is made for technical assistance to Mrs. Bessie L. Jacobson, research associate, The University of Rochester Atomic Energy Project, in making the electron micrographs; and to Miss B. Kindig, of the Research Laboratories of the Eastman Kodak Company, for the ultrasonic dispersion of the various preparations.

mineral and organic substances. The inorganic particles have not been seen hitherto.

Since the advent of the electron microscope the range of possible visualization has increased to the 20-to-100-A range, in which the individual inorganic units of bone should be seen. Henschen (*5, 6*) stated that bone in the mineral phase exists as crystals 2×10^{-6} to 2×10^{-8} cm long. Cagliotti (*4*) suggested 10^{-6} cm as the crystal length. (Bale, Hodge, and Warren [*1*] postulated that the crystal size in dentine is 2.4×10^{-6} cm and in enamel 2.7×10^{-5} cm. Moeller and Troemel [*7*] gave 10^{-4} cm as the size of enamel particles and 10^{-5} to 10^{-6} cm as dentine particle size.)

FIG. 1. Micrograph of fresh tendon, agitated in chemically pure water in Waring Blendor for 10 min and subjected to ultrasonics at 400 kc for 10 min. Magnification × 62,500.

During the past seven months satisfactory methods of preparing bone samples for the electron microscope were developed by the authors. Three methods were found most useful:

(1) Fresh cortical bone is cleaned and then scraped with a sharp knife. The scrapings are placed in a Waring Blendor in 100 ml of chemically pure distilled water (in ampules). This sample is blended for 10–15 min and then poured into a meticulously cleaned test tube. The fluid appears gray and cloudy, owing to a fine dispersion of the bone scrapings. A drop of this fluid is placed on an electron microscope specimen screen which was previously coated evenly with silicon (*3*). Similar treatment of tendon shows that it leaves collagen fibers intact and that striations at 640 A, as described by Schmitt (*8*), are clearly seen. Therefore, this treatment should not destroy the collagen in bone (Fig. 1).

(2) Bone is cleaned and autoclaved at 27-lb pressure (269.8° F) for 2 hr (*4*). The bone is then washed in distilled water and placed in the Waring Blendor in 100 ml chemically pure distilled water for 10–15 min. The

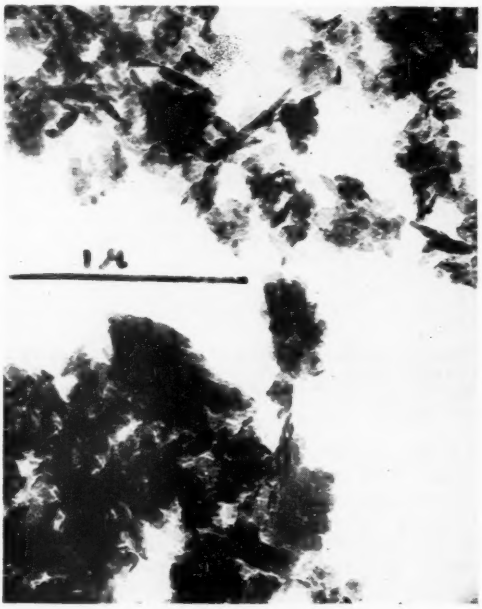

FIG. 2. Micrograph of cortical bone, autoclaved 2 hr at 27 lb (270° F), agitated in Waring Blendor for 15 min. Magnification × 34,500.

organic matter having been largely removed, the collagen fibers are not seen in these samples. The fluid appears cloudy gray and a drop of it is placed on a specimen screen, previously silicon-coated. The micrographs obtained are uniformly clean and, when properly focused, the crystal units of the bone are plainly seen, most of the crystals remaining in clumps of characteristic appearance (Fig. 2).

(3) Samples obtained by the two preceding methods are subjected to ultrasonics, approximately 400 kc, for 5, 10, and 15 min (*2*). In our experience, collagen so resonated for more than 10 min appears to disintegrate. Therefore, when attempting to observe collagen fibers in bone, the sample is resonated for shorter periods but when inorganic crystals are to be observed, longer periods (15 min) have been used.

The best preparation for viewing the inorganic portion of bone is obtained by autoclaving clean bone for 2 hr, blending for 20 min, and finally resonating for 15 min. By these procedures a fine, clean dispersion of the crystalline units of inorganic bone is obtained for observation (Fig. 3). Cancellous bone so treated produced

fair preparations but it was more difficult to find clean fields, probably due to the larger amount of organic material present. Deciduous teeth were crushed, autoclaved, blended, and resonated. Glycol-ashed bone was blended and subjected to ultrasonics. Adequate micrographs were obtained in both instances. Bone thus prepared shows the picture of normal bone in the x-ray diffraction pattern.

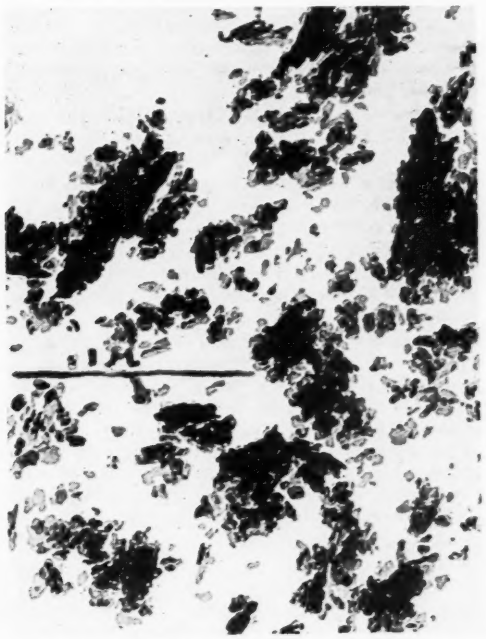

FIG. 3. Micrograph of cortical bone, autoclaved 2 hr at 27 lb (270° F), agitated in Waring Blendor for 15 min, and subjected to ultrasonics at 400 kc for 15 min. Magnification × 34,500.

These methods are being used to investigate the submicroscopic structure of bone. A paper is being prepared which will detail the findings, interpretations, and conclusions obtained from electron micrographs of material prepared by these methods.

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Arrest of Development of *Plasmodium gallinaceum* in Mosquitoes (*Aedes aegypti*) by Radiation Effect of P^{32} [1,2]

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During the course of experiments on the radioactive tagging of sporozoites of the avian malaria parasite *Plasmodium gallinaceum*, it was observed incidentally that ingestion of P^{32} by host mosquitoes during the period of extrinsic incubation caused development of the parasite to be arrested. The present report deals with this observation.

One hundred fifty *Aedes aegypti* were allowed to engorge on chicks that were infected with *P. gallinaceum* and that showed many gametocytes in their peripheral blood. Thereafter these mosquitoes were provided daily with 5% glucose solution containing radioactive sodium acid phosphate, the total radioactivity approximating 30 mc. This material was soaked in a cotton pledget which was moistened occasionally with water. One hundred other mosquitoes, exposed to infection at the same time and in the same way, were subsequently provided with glucose solution only. Radioactivity measurements were made on a counting-rate meter (*1*) employing a thin mica window, bell-type Geiger-Müller tube.

Nine days following the blood feeding, ten mosquitoes from each group were dissected for determination of the presence of oöcysts in their stomachs; all ten of those receiving glucose and P^{32} contained oöcysts, as did eight of those receiving glucose alone (see Table 1). No difference in average numbers or stage of development of oöcysts was noted in the two groups of mosquitoes. Five days later, mosquitoes from each group were dissected to determine the presence of sporozoites in the salivary glands. No sporozoites were found in 93 mosquitoes given P^{32}, whereas 11 out of 15 given glucose alone showed these forms (see Table 1).

Measurements of radioactivity were made on the salivary glands of 87 of the mosquitoes given P^{32}. These measurements were corrected for decay to the time of first feeding of the P^{32} glucose solution. The lowest activity for a salivary gland was 334 cpm, the highest was 14,000 cpm, and the average of the 87 was 2,400 cpm. In the absence of a reliable figure for the average amount of tissue involved in the salivary glands, it is difficult to

[1] This study was carried out at the suggestion of Dr. Robert Briggs Watson, then of the Tennessee Valley Authority, who arranged for the partial financial support from that source. Miss Lois Seamans, of the Tennessee Valley Authority, performed many of the final salivary gland dissections.

[2] The radioactive phosphorus (P^{32}) used in this study was prepared in the cyclotron of the Massachusetts Institute of Technology.

TABLE 1

RESULTS OF FEEDING P^{32} TO *Aedes aegypti* DURING PERIOD OF EXTRINSIC INCUBATION OF *P. gallinaceum*

Mosquito lot no.	No. fed on gametocyte carrier (10-26)	Feeding during period of extrinsic incubation	Dissected for oöcysts (11-4)		Dissected for sporozoites (11-9)	
			No.	Positive	No.	Positive
544 A	50	Glucose solution only	5	3	4	2
691 A	50	Glucose solution only	5	5	11	9
688 A	50	P^{32} + glucose	5	5	36	none
692 A	50	P^{32} + glucose	5	5	25	none
692 B	50	P^{32} + glucose	none	..	32	none

estimate the total radiation delivered to the gland itself. The efficiency of our Geiger counter could be estimated as being approximately 20%, and this would mean that there were in the vicinity of 12,000 disintegrations per minute in the average glands during the early part of the feeding process. Owing to the extremely small amount of tissue involved, this would suggest a very high equivalent roentgen dosage. On the other hand, in spite of such a relatively high degree of radioactivity, it was surprising that there were no apparent deleterious effects on the mosquitoes themselves during the period studied. No gut examinations were carried out on the 14th day, and therefore there are no data as to presence or absence of oöcysts at this time in the 93 mosquitoes that showed no sporozoites in the salivary glands.

It appears that the amount of radiation in the salivary glands and/or the mosquito as a whole was sufficient to arrest development of the parasites during the oöcyst stage.

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Toxicity to Mice of Chlordane Vapor and Solutions Administered Cutaneously[1]

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The toxicity of DDT to mammals has been rather thoroughly investigated (*2, 4, 7–9*), and it is now known that acute intoxication causes nervous disorders, and chronic intoxication results in fatty degeneration and necrosis of the liver. The newer insecticide, Chlordane,[2] however, has received much less attention. In general, its action is similar to that of DDT, but it is more readily absorbed through the skin (*1, 2, 6, 8*). Like DDT, it causes hepatic necrosis in chronic intoxication (*4, 6–10*). The present investigation was instituted to determine the effects of long-continued application of small quantities of Chlordane to the skin, and also to discover the possible toxicity of its vapor.

Five groups of virgin female Swiss albino mice were used in the experiments: Ten mice received no treatment and served as a control group; 16 mice received cutaneously 0.01 ml of odorless kerosene (Deobase) daily for 5 days per week; 16 mice received cutaneously 0.01 ml of 2% Chlordane solution in odorless kerosene (7.4 mg of Chlordane per kg of body wt per day) daily for 5 days per week; 16 mice received cutaneously 0.04 ml of 2% wettable powder suspension of Chlordane daily for 5 days per week; 60 mice in four subgroups were exposed to Chlordane vapor for different periods of time.

The amounts selected for application to the mice corresponded to doses which a man might receive were he to have his hands and arms wetted to the elbows. Because of the higher surface tension of the wettable powder suspension, more of this than of the kerosene solution is required to effect the same wetting. The solutions were applied from a micropipette to the intrascapular region of the mice. When applied at that spot, the solutions are difficult or impossible for a mouse to remove by itself. Extended observations showed that the mice made no effort to lick each other after one or two tastes of the kerosene or Chlordane solutions. Thus the materials entered the body through the skin and were not ingested. Since some of the Chlordane evaporated from the skin, there must have been some inhalation of the vapor, but probably not in appreciable amounts.

The cutaneous treatments were continued for a total of 20 weeks, 5 days per week. The total amount of kerosene or Chlordane-kerosene solution applied to each mouse was 1 ml and it contained 20 mg of Chlordane (740 mg/kg body weight). The total amount of Chlordane applied to each mouse in the group receiving applications of the wettable powder was four times this. Every month one mouse from each group, selected at random, was sacrificed for autopsy, and the tissues were fixed for histological study. Only the livers have been studied histologically so far.

For tests of vapor toxicity, two types of setup were used. In the first, 16 mice were housed in a wire-mesh cage supported in a box (12 in. × 20 in. × 36 in.) without touching the sides. This box was covered with three pieces of glass with 4-in. spaces between for ventilation. Once every 3 weeks, a strip about 2 in. wide around the inside of the box was painted with about 5 g of Chlordane. The concentration of Chlordane vapor was estimated at about 25% saturation at the start of the experiment, and as a result of accumulation of material on the strip, at about 50% saturation at the conclusion. Since quantitative tests for Chlordane vapor in air do not exist, these are only approximate estimates. The amount applied to the box was considerably higher than that which would be applied in pest control practice, and

[1] Authorized for publication as paper No. 1542 in the Journal series of the Pennsylvania Agricultural Experiment Station. This work was financed by a grant from the John G. Vogel Memorial Fund.

[2] The Chlordane used in these experiments was kindly supplied by the Julius Hyman Company, to which we wish to express our appreciation.

this was only partially offset by the fact that ventilation of the box was greater than that of an ordinary room. In the second setup, mice were exposed in a treatment chamber to air which had been bubbled through Chlordane in a saturation chain. Twenty mice were exposed to this continuously, 12 were exposed for 15 hr every day, and 12 were exposed for 9 hr every day.

A refined grade of Chlordane, containing 60%–75% Chlordane and 25%–40% related compounds also insecticidal in nature, was used in the experiments. This and the kerosene used as the solvent are standard products present in household insecticidal sprays. The carrier in the Chlordane wettable powder was Attaclay.

In view of the report by Ingle (*6*) that rats treated with Chlordane convulsed when subjected to intense auditory stimulation, the animals were tested every 20 days for susceptibility to "audiogenic" seizures. The technique was like that used by Hall (*5*) in his work on mice. A mouse was placed in a metal washtub to which an electric doorbell was fastened. After a period of 1 min, during which the mouse usually explored the tub, the bell was sounded for 75 sec or until the animal convulsed. The intensity of sound produced in the tub was 102 ± 2 db (relative intensity 10^{-16} watts/sq cm) at the periphery and 95 ± 2 db at the center, with the major frequency components between 0.7 and 1.2 kc.

The seizure pattern is striking. When the bell is turned on, the susceptible mouse cringes at the side of the tub. After a variable period of time, the mouse starts a series of short jerking runs. Finally it breaks into a frenzied run around the tub and after a few circuits of the tub falls over in a coma which usually culminates in death if the sound is not turned off. In our experiments, an effort was made to stop the bell just as soon as it was obvious that the wild running fit had started, so that the mice could be saved for further testing.

Although the physiological and psychological mechanisms involved in the seizure pattern are still obscure, it seems certain that susceptibility to seizure is a rough estimation of nervousness in the animals (*3, 11*). This gives us a method for detecting possible toxic effects on the nervous system before these become incapacitating.

The mice in the control group and in the group receiving applications of kerosene gained weight normally and appeared at all times in good health. The kerosene caused a loss of fur at the site of application, but there was no dermatitis. There were no deaths other than routine sacrifices. The livers of mice in both groups were normal both macroscopically and microscopically. In seizure tests, two mice in each group convulsed at the first two tests, but only one mouse, this in the kerosene group, continued to have seizures after the second test. Mice of this strain lose the tendency to seizure with increasing age; therefore, these results may be considered as representative of normal mice. The seizure results correspond well with those obtained in our laboratory with mice of the same strain being tested in a totally different experiment.

Mice in the groups receiving applications of Chlordane, either in the kerosene solution or the wettable powder suspension, reacted quite differently. After about 3 weeks of application, the mice became distinctly excitable, running to and fro in the cage without seeming purpose. They would jump from almost any height and became difficult to handle. Weight gains were normal, and appetites were unimpaired, however. Seven of the Chlordane-kerosene group and nine of the wettable powder group died before the end of the experiment. On autopsy, these were found to exhibit a rather typical liver damage. The kerosene solution brought about loss of fur, probably the result of the kerosene, and a dermatitis of variable severity characterized by roughening of the skin with local areas of bleeding and ulceration. The wettable powder suspension, on the other hand, caused only slight loss of fur and little or no dermatitis. The kidneys and liver of mice treated for 10 weeks or more appeared lighter than normal with white blotches, the lungs were occasionally hemorrhagic, and other organs appeared normal. Histologically the livers of mice from both groups showed a typical centrolobular necrosis after about 10 weeks of treatment, with the left lateral lobe most severely affected.

The mice in the treated groups exhibited a much higher percentage of seizures than normal mice. In the kerosene-Chlordane group, the number of seizures rose steadily from the start of the experiment; after 6 weeks of treatment the level of incidence was greater than 30%, and it remained over that for the rest of the experiment, the highest percentage being 45%. Three mice died in seizures in this group, the only mice which died during testing. Since in this group every mouse which convulsed continued to convulse in all subsequent trials, these three, which died early in the experiment, would probably have been among the individuals which had seizures in later tests, and thus the percentage incidence would undoubtedly have been about 45%–60%. The seizures of treated mice also were preceded by a shorter latent period than those of normal mice, and they were more severe. In the wettable powder group, the incidence of seizures remained about normal until after 9 weeks of treatment. Then this climbed to about 50%, where it remained until the end of the experiment. As a critical test of the effects of Chlordane wettable powder suspension on seizure incidence, mice about 40 days old were tested, and 7 of these which did not exhibit seizures were selected for treatment with the suspension. These young mice, all of which were negative at the start, showed 70% seizures following 3 weeks of cutaneous applications. There was no apparent correlation between the incidence of seizures and liver damage.

The mice in the group breathing a relatively low concentration of Chlordane vapor showed, after a few weeks, a characteristic loss of activity and muscular coordination. Weight gains and appetite, however, were normal. All the mice were dead after 16 weeks of exposure, half the deaths occurring one by one before the fifteenth week, and the remaining half immediately following renewal of the coating of the strip in the box at that time. There was evidence of liver damage after 6 weeks of exposure. Histologically, the liver presented the same picture of necrosis as was found in the other treated groups.

In sound tests, the group exhibited the normal low percentage of seizures up to 9 weeks of treatment. Following that, the percentage rose sharply to 50% just 2 weeks before all the mice died.

The mice in the groups breathing air saturated with Chlordane reacted quite differently. They immediately ceased feeding and drinking and huddled together, seeming loath to move at all. They apparently became blind and within relatively few hours lost all power of coordination. All the mice in the group exposed continuously died within 4 days, four of the 20 dying during the first day. The mice in the groups exposed for 15 hr/day and 9 hr/day were exposed for only 4 days. Half of the 15-hr group were dead at that time, and the others died within a few days. Two of the mice in the 9-hr group were dead at the end of 4 days (36 hr of exposure), and all but four died within the next 10 days. This confirms the statement of Radeleff (*10*) that animals "poisoned by Chlordane do not seem to recover, once they have manifest toxic symptoms." There were no observable anatomical differences between these mice and normal mice, except for extreme emaciation in mice which lived for some days. No sound tests could be given because the mice survived too short a time and seemed incapable of moving about with rapidity after 6 hr–8 hr of exposure to the vapor.

In general, results of this study indicate that Chlordane is very similar to DDT in its toxic action in mammals. The first system affected is the nervous system, and nervous symptoms predominate in acute toxicity. In chronic intoxication, however, the liver seems to be most affected. We were unable to determine to our satisfaction whether Chlordane accumulated in the fat of the mice or not. Possibly the cumulative toxicity is owing merely to destruction of the liver cells, along with effects on other organs of the body such as the kidneys.

Because of the widespread use of Chlordane in structural pest control, the rather striking toxicity of the vapor is significant. In this particular, Chlordane differs from DDT, just as it does in the apparent relative ease with which it is absorbed through the unbroken skin. A surprising feature is the relatively high toxicity of wettable powder preparations, since it is usually assumed that this type of preparation is less readily absorbed than kerosene solutions. All these results indicate that repeated exposure to Chlordane preparations on the skin or continued inhalation of the vapor may be deleterious.

Another striking point is that the treated animals gained weight normally, and except for greater irritability than the controls, seemed in good health. If transposition of results on mice to man is permissible, this indicates that the general level of health, appetite, weight maintenance, and the like would be a poor index of early chronic intoxication by Chlordane. The established fact that the chlorinated hydrocarbon insecticides have a similar cumulative action makes it imperative that clinical tests for detection of early intoxication in man be developed.

In experimental animals, the method of "audiogenic" seizures seems promising as a test for early intoxication. From our results with Chlordane, it is seen that the incidence of "audiogenic" seizures in a population of treated mice rises rather sharply a few weeks before clinical symptoms and deaths appear. With proper standardization of the test situation and with selected mice, this test may provide a good indication of early intoxication.

Finally, the results suggest that Chlordane may have value as a rodenticide. Since it is toxic to animals when absorbed through the skin and lungs, as well as when ingested, it might be used under favorable conditions for control of mice and possibly rats.

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Stability of the Adenosinetriphosphatase System in Animal Tissues[1]

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In the course of experiments on the stability of respiratory enzyme systems in beef tissues obtained from carcasses of different grades and aged for varying periods, the stability of the adenosinetriphosphatase (ATP-ase) system in intact tissues was investigated. Data on the nature and occurrence, metabolic function, and specificity of this system have been reviewed (*2, 3*); however, little attention has been devoted to studies on the stability of the system in intact tissues stored for varying periods of time after the animals are killed. In the present study the ATP-ase activity of animal tissues stored at −2° C and at +5° C for periods up to 15 days was investigated.

Preliminary experiments were conducted with rat tissues and the study was then extended to beef muscle tissue. The procedure used for determining the ATP-ase activity of the tissues was essentially that described by Umbreit, Burris, and Stauffer (*5*). Young adult rats that were fed stock ration were killed by decapitation. Approximately 1 g of muscle tissue, and in certain experiments liver and kidney, were removed and prepared

[1] This work was supported in part by a contract with the Production and Marketing Administration, U. S. Department of Agriculture, under the Research and Marketing Act.

for the ATP-ase assays. The tissues were homogenized in a Waring Blendor for 5 min and each tissue was assayed at levels of 1 and 2 mg of fresh tissue per assay. The equipment used was kept cold during preparation of the tissues and ice was added during the blending period.

After the tissues were obtained for determination of the ATP-ase activity, the remainder of the carcass was wrapped in moistened paper towels and stored at either −2° C or at +5° C. Samples of tissue were removed 2, 4, 8, or 15 days later and the ATP-ase activity was determined. In some experiments two different samples of muscle tissue were taken from the same carcass on the same day, and the values obtained for the two samples were in good agreement.

TABLE 1

ADENOSINETRIPHOSPHATASE ACTIVITY OF RAT TISSUES AS INFLUENCED BY STORAGE CONDITIONS*

Tissue or organ	Storage temperature	Time of storage (days) 0	2	4	8	15
Rat No. 1						
Muscle		14.8	15.0	13.0	15.3	16.2
Kidney		9.9	12.4			
Liver	−2° C	8.1	7.8	6.9	6.4	5.2
Rat No. 3						
Muscle		13.4		12.3	14.4	11.2
Liver		6.5		5.9	5.0	3.3
Rat No. 2						
Muscle		14.1	12.2		15.5	
Kidney	+5° C	12.2	12.8			
Liver		7.5	8.0			
Rat No. 4						
Muscle		15.8		11.9	13.3	

* Values expressed as μg phosphorus liberated per mg of fresh tissue in 15 min at 37° C (*1*).

TABLE 2

ADENOSINETRIPHOSPHATASE ACTIVITY OF BEEF MUSCLE TISSUE AS INFLUENCED BY STORAGE CONDITIONS*

Sample†	Storage temperature	Time of storage (days) 0	5	9	15
No. 1		9.3	9.0	8.8	9.0
No. 2	−2° C	7.9	8.1	6.9	7.2
No. 1A	+5° C	7.3	8.5	8.5	8.7
No. 2A		7.3	7.1	7.8	7.2

* Values expressed as μg phosphorus liberated per mg of fresh tissue in 15 min at 37° C.

† Samples 1 and 1A were obtained from the same carcass and were adjacent sections, 1½ in. thick of the *longissimus dorsi* muscle. A similar pairing was made for samples 2 and 2A from another carcass.

The rib-eye muscle (*longissimus dorsi*) from the 11th and 12th rib cut was obtained from steer carcasses that weighed 631 and 637 lb. These samples were obtained 24 hr after the steers were killed and the rib-eye muscle was then dissected free of fat and connective tissue. Two samples were prepared from each carcass; one was stored at −2° C, and the other at +5° C. The samples were approximately 1½ in. thick and were wrapped in paper and stored as indicated. The outer portions of the muscle were removed prior to sampling and 3–4-g samples were taken for ATP-ase assays at 0, 5, 9, and 15 days of storage.

The ATP-ase system was found to be essentially stable in both intact rat and beef muscle tissues during storage for periods up to 15 days with the test conditions used (Tables 1 and 2). The slight increases in activity after storage may have been due to a reduction in water content during storage of the tissues. Results obtained for tissues stored above freezing (approximately +5° C) were essentially similar to those obtained for tissues stored at −2° C in that after 8–15 days no appreciable changes in ATP-ase activity had occurred. Some reduction in the ATP-ase activity occurred in liver as evidenced by the results obtained with tissues stored at −2° C.

Values obtained for rat muscle, kidney, and liver were somewhat lower than those reported by DuBois and Potter (*1*). No comparable data are available for beef tissues. The technique of homogenization used in the present work may not have been as effective in rupturing the cells as that used by these workers. The ATP-ase activity was not increased by increasing the homogenization time to 10 or 15 min. The ATP-ase activity of beef muscle was lower than that obtained for rat muscle.

It is significant, therefore, that the ATP-ase system in these intact tissues is essentially stable for a considerable period after the animal is killed. This is in contrast to the instability of certain other enzyme systems such as the oxalacetic acid oxidase system (*4*).

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A Modern Periodic Chart of Chemical Elements

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Since the discovery and elucidation of the actinide series of elements, a reexamination of the perennial problem of the position of the rare earths (and now the actinides) in the periodic chart of chemical elements appears to be desirable. The disposition of these series is far from obvious. Emeléus (*3*) and others have pointed out that the actinides are quite analogous to the lanthanides, but Anderson (*1*) has emphasized their resemblances to the other elements. The accompanying chart (Fig. 1), a development of one published by the author (*2*) in 1933 and recently republished (*5*) in a slightly modified form, but with a much more extensive treatment of the two

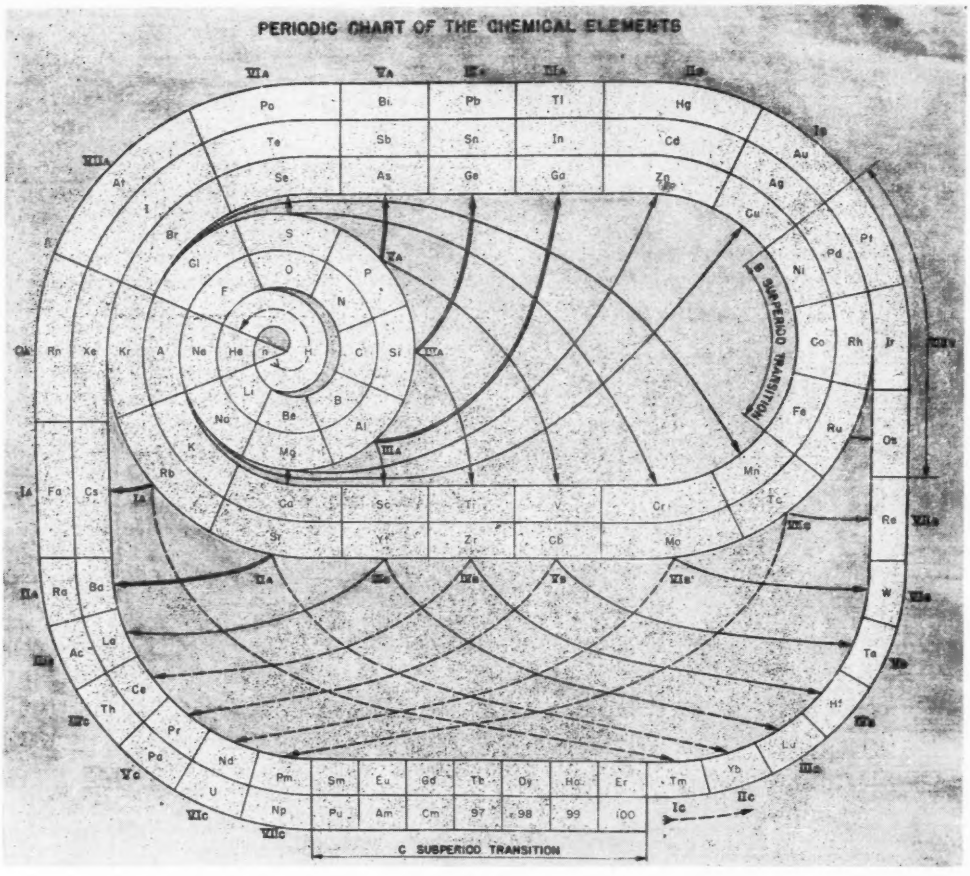

FIG. 1.

series in question, is submitted as a satisfactory solution to the problem.

The most important difference between this and other charts is the division of the groups of elements into three types of groups (instead of the usual division into main and subgroups), resulting from the recognition of three types of subperiods. An A subperiod is that part of a period in which the electron shells of the elements have each been completed by addition of an *s* or *p* electron; the shells of B subperiod elements have each been completed by addition of a *d* electron; and C subperiod elements are those whose shells have been completed by addition of an *f* electron. The A, B, and C groups are defined in the same way. An A subperiod then consists of seven elements plus one transition element (the inert gas); a B subperiod, inserted between IIA and IIIA, has seven elements plus a transition group of the three iron group elements; and a C subperiod, between IIIB and IVB, comprises seven elements and a transition group of seven. Hackh (*4*) pointed out that the consecutive resemblances among elements in a B subperiod approach in importance the periodic relationships, and this phenomenon is even more pronounced in the C subperiods, where resemblances among elements in the series are usually more obvious than similarity to elements in other periods.

The chart presented has the following advantages. It appears to be as simple as possible, consistent with the relationships to be expressed. The idea of continuity is emphasized by the continuous spiral arrangement, and the complex periodicity of the elements is clearly shown. It treats hydrogen logically, as a unique element, putting it at the head of both the IA and VIIA groups. At the same time, it makes a place for the neutron at the beginning of the series and as the first of the inert gases. It separates the A and B groups, but shows their relationships by the tie-lines. (A double tie-line leads to an A group, a single to a B.) The treatment of the lanthanides and actinides is rational and unforced, emphasizing their similarity, but clearly indicating their rela-

tionships to the other elements, (a dotted tie-line leads to a C group) so that such valences as Ce^{+4}, Pr^{+5}, U^{+6}, and Yb^{+2}, appear logically to be expected.

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Dry Mounts of Amphibian Cleavage Stages

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Use of dried vertebrate embryological materials for demonstration has recently been reported (*1*, *2*). Such methods have been rather widely used but not always reported in the literature.

The use of formalin-preserved amphibian cleavage stages in embryology presents certain difficulties in handling and orientation, especially for students in large classes, and when there is lack of adequate dissecting scopes or light. The method to be described is simple and has proved helpful in the study of amphibian cleavage by classes at Duke University.

Fig. 1.

Formalin-preserved material, previously fixed in Smith's fluid or 10% formalin, is washed in tap water for 2 hr. Jelly and vitelline membranes are then removed by rolling on paper towels. Complete removal of vitelline membranes is important in order to avoid many surface reflections. Bleaching is helpful, and is the next step in the method. Standard techniques such as use of hydrogen peroxide, Javelle water, or hypochlorite solutions are satisfactory. Bleaching is followed with washing in tap water for at least 1 hr and dehydrating through a series of alcohols going from absolute alcohol to xylene, where the material may be stored (or it may be stored in 85% alcohol). The material is put on a paper towel and air-dried for 5 min. It is then ready for mounting or storage.

There are several methods for mounting, but we have found that fastening the material to the tips of paper or clear plastic triangles by means of household cement is successful. The triangles are first pierced with insect pins in a manner similar to that used in gluing small insects. Plastic triangles have the advantage of being usable again in case the specimen breaks.

Some of our dried mounts prepared in this way have been in use for 4 years and show no sign of change. They can be stored in insect boxes while not in use. With a minimum of light and low magnification, the cleavage furrows stand out clearly (Fig. 1). To facilitate handling, the pins can be placed on pieces of balsa or cork when in use. Hemisections of blastulae can be mounted in the same way as cleavage stages.

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Rooting of Haden Mango (*Mangifera indica* L.) Leaf-Bud Cuttings

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One of the factors retarding the development of a large scale mango industry in Florida is the lack of knowledge concerning the theoretical aspects of mango propagation and selection. The present paper introduces a new method of propagation which may be helpful in elucidating these problems.

At present, the varieties of mangos grown in this state are propagated by graftage, inarching, and, rarely, by air-layering (marcottage), of scions of known varieties on seedling rootstocks of unknown parentage (*1*, *3*, *15*, *16*). The lack of uniformity in these stocks—some of which are grown from polyembryonic seeds, turpentine, apple, and No. 11 being the commonly used varieties; and others from monoembryonic seeds, such as Haden and Saigon—may be a contributory factor in the tendency toward biennial bearing and other deleterious characteristics apparent in most grafted plants regardless of variety (*1*, *3*, *16*).

In Florida, the chief emphasis in mango propagation has been on selection of new varieties from chance seed-

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[2] The author is indebted to Dr. David Fairchild for permission to experiment with his mango trees; to Mrs. Marion Fairchild for helping in editing the paper; to Dr. Taylor R. Alexander, chairman of the Department of Botany, for his cooperation; and to Mr. A. B. Sutton, of the City of Miami Municipal Nurseries, for supplying the coconut husk compost.

lings of trees of known worth (*17, 25, 33, 34, 43, 44*), and in the development of methods of graftage and budding to supplant the slow, costly inarching procedure, which is still being used to some extent (*1, 4, 18, 22, 23, 24, 29, 30, 37, 38, 42, 45*).

Little progress has been made on the problem of clonal selection of mangos for two reasons, the absence of serious incompatibility problems due to graftage, using seedling stocks (*13, 20, 29*), and the difficulties encountered in propagating clones on uniform rootstocks (*22–24, 37*). Air-layering, although one of the common older methods in the East Indies, has been used sparingly in Florida for quantity production. The literature on mango propagation since 1900 attests the paucity of successful plants grown from cuttings (*3*). In 1940 Guha-Thakurta and Dutt published the results of their treatments using 1% indoleacetic acid on cuttings from juvenile growth of seedlings (*9*). Although this work was a step in the right direction, it had little practical significance for clonal rootstock selection purposes until means could be found for rooting cuttings taken from mature, bearing trees of known characteristics. The reports of Guha-Thakurta and Dutt (*10, 11*), Gardner and Piper (*8*), and others (*39–41*) indicate that very low percentages of rooting with stem-cuttings or gootes (mareottes) from mature trees were obtained.

The problem of rooting of cuttings is discussed in a general way for pome fruits by Cooper and Stoutemeyer (*5*), and by others (*12*). The rooting of stems of young seedlings of woody plants suggests that all seedlings pass through distinct juvenile and mature growth phases. In buddings or inarches of trees, the scion is ordinarily made from wood of shoots in the mature growth phase, and in a number of species it is impossible, or possible only under certain circumstances, to induce juvenile growth on the scions. The mango obviously belongs to this group (*8, 10, 11, 39–41*). The new shoots found along the margin of wounds on limbs and stems broken or damaged by hurricanes in Florida, however, resemble in their external characters those exhibited by seedling stems in their juvenile stages. Furthermore, cases are known in the Haden and other commercial varieties where such shoots developed roots from the callused wound margin from which they had sprouted (*36*). Whether these shoots arise from adventitious or latent buds is not known. These discoveries encouraged experimentation with this type of new growth. The vertical or near vertical growing parts of these regeneration shoots were chosen for study. It seemed undesirable, however, to use stem cuttings, since relatively few could be made, owing mainly to the fact that the shoots developing from wounded limbs tend to put out laterals very quickly. The success of other workers with rooting leaf-bud (mallet) cuttings suggested the possibility of using this method (*2, 5, 14, 28, 31*).

The propagation frames used in the experiments reported here consisted of aluminum trays (24 in. × 16 in. × 6 in. deep) with drainage holes in the bottom. These were filled with sieved coconut husk compost (a material commonly used for the purpose in the Netherlands East Indies), placed in an open propagation bench at the University of Miami main campus, and kept under constant spray from fan-shaped nozzles.

FIG. 1. Leaf-bud cuttings of the Haden mango, treated with indolebutyric acid 10,000 ppm, showing various stages of root development. Bottom leaf-bud cutting shows callusing and first root development. The middle and upper ones show activity of the dormant axillary bud. Photo by Fred B. Fleming, University of Miami photographer.

From Haden mango trees, leaf-bud cuttings from the firm green part of wound shoots were made in June, 1949, care being taken to see that a chip of wood remained attached to the underside of the bud. The cuttings were washed in running water 30–45 min to remove exudate from the cut edges of the bark. Immediately thereafter the mallet portion of the cuttings, including the axillary bud, was immersed for 5 sec in an indolebutyric acid solution (10,000 ppm in 50% methanol). The cuttings were then superficially planted in the propagating trays. There was full morning sun with light shade the rest of the day. No precautions were taken to screen the trays from high winds or torrential summer rains. The continuous water spray served to reduce transpiration and to lower the temperature of the rooting medium; it seldom exceeded 27° C even during dry hot days (*7, 8, 32*).

After 6 weeks in the rooting medium the cuttings were examined for sign of roots. Of the treated ones, 75% were rooted or had started to root, with buds also showing signs of growth (Fig. 1). Many of the roots had grown through the drainage holes in the trays and were broken off upon removal. With an untreated control series, most of the cuttings had died and of those alive, none showed signs of root formation when examined at the end of 6 weeks.

Additional experiments are now in progress to determine the influence of time of year and cold shocks on the rooting of cuttings similar to those described, the hardening off of rooted cuttings, the optimum conditions for transplanting, and the behavior of varieties other than the Haden mango.

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Niacin Content of Waxy, Sugary, and Dent F_2 Segregating Kernels in Corn[1]

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The existence of a direct relation between sugary endosperm and high niacin content of the corn kernel has recently been confirmed by Cameron and Teas (*3*), after having been suggested by several other workers (*1, 2, 4, 5*). It has been indicated (*6*) that there may also be a relationship between waxy endosperm and high niacin content, but no data have been presented to support this suggestion.

As part of a study of the inheritance of niacin content in corn, waxy, sugary, and dent F_2 segregating kernels of a cross between a high niacin sugary line (mean niacin content 48.3 μg/g) and a low niacin waxy line (mean niacin content 18.0 μg/g) were analyzed. The data obtained appear to be of value in clarifying the relationship between endosperm type and niacin content in corn, and are therefore presented in this paper.

Eighteen self-pollinated ears from F_1 plants of the waxy-sugary cross were available for analysis. The F_2 kernels on each ear were separated according to their endosperm type. Counts showed a close agreement with the expected segregation ratio of 9 dent: 3 waxy: 4 sugary. Fifteen kernels of each endosperm type were taken from each ear. An effort was made to select kernels of uniform size within each sample. The 15-kernel samples were then assayed for niacin content.

Niacin determinations were made by the microbiological method of Snell and Wright (*7*) after hydrolysis of samples in 1 *N* H_2SO_4 for 30 min at 120° C. Hydrolyzates were adjusted to pH 6.8, filtered, and assayed in the conventional manner. All results are given on a moisture-free basis.

Table 1 shows the mean niacin content of the waxy, sugary, and dent kernels, as well as the range in niacin content found among ears within each endosperm type. The average niacin content of the sugary kernels was about 23% higher than that of the waxy kernels, while the waxy kernels in turn were about 18% higher in niacin than the dent kernels. Differences in niacin content between each of the three endosperm types greatly exceeded those required for statistical significance at the 1% level. It is also significant that in each of the 18 ears sampled, dent kernels were lowest, waxy kernels intermediate, and sugary kernels highest in niacin content. Mean niacin content of individual ears also differed significantly, although the differences between ears tended to affect

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TABLE 1

NIACIN CONTENT OF SUGARY, WAXY, AND DENT F_2 SEGREGATES OF CROSS BETWEEN SUGARY AND WAXY LINES OF CORN

F_2 endosperm type	Niacin content, μg/g	
	Mean of endosperm type	Range within endosperm type
Sugary	33.8	26.5–42.0
Waxy	26.0	19.5–32.5
Dent	21.4	16.0–26.8
Differences between mean niacin values necessary for significance:	5% level—1.5 μg/g	
	1% level—2.0 μg/g	

the niacin content of all three endosperm types to about the same degree, as indicated by the correlations between them (Table 2).

TABLE 2

CORRELATIONS BETWEEN NIACIN CONTENT OF DIFFERENT ENDOSPERM TYPES BORNE ON SAME F_1 EARS

Comparison	Value of correlation coefficient
Sugary : waxy	+0.758*
Sugary : dent	+0.793*
Waxy : dent	+0.821*

* Exceeds value required for significance at 1% level.

With present information, the apparent relationship between endosperm type and niacin content cannot be satisfactorily explained. Genetic linkage has been suggested. The results reported here are not fully in accord with this idea. Sugary endosperm came into the cross with high niacin content, and the extracted sugary segregates were high in niacin. However, waxy endosperm came into the cross with low niacin content, yet the extracted waxy segregates were higher in niacin than the waxy parent and also higher than the dent segregates. Also, the data of Cameron and Teas (*3*) clearly indicated that the high niacin content of sugary kernels was not the result of linkage, since sugary kernels produced by the action of either of the independent genes su_1 and *du* were equally high in niacin. Therefore, it appears that a more likely explanation than linkage is that there is a direct influence of endosperm type on the niacin content of the corn kernel.

Richey and Dawson (*6*) have suggested that this influence may be related in some way to the effects of endosperm type on kernel size. Unpublished data of the present authors indicate, however, that there is no close relationship between kernel size and niacin content, at least in genetically similar material. As suggested by Cameron and Teas (*3*), it appears more probable that vitamin-carbohydrate interrelations in the developing corn kernel are involved, though little is known of the specific nature of these interrelations.

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Relation of Strength of Sediments to Water Content and Grain Size

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Strength of sediments is of fundamental interest to geologists and foundation engineers. Water content is a basic factor affecting strength and has been used for many years as a guide to the relative strength of sediments. Water content, however, as many people have pointed out, is not an exact index, because other factors also influence strength. Among these other factors, grain size, because of its pronounced effect upon the general characteristics of sediments, should exert a significant influence.

Extensive data on the sediments of San Francisco Bay have given the authors an opportunity to investigate the relationship of strength to grain size and water content. More than 400 samples of silt and clay were available for study. Sands—that is, sediments having a median diameter, D_{50}, greater than 64 μ—were excluded. Samples were distributed fairly evenly between two Quaternary formations separated by an erosional disconformity.

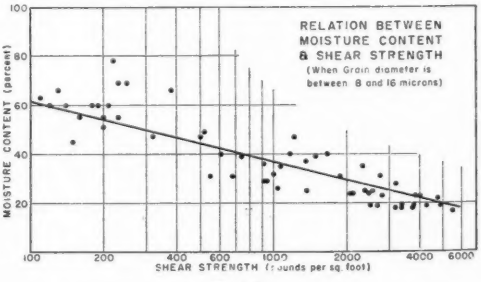

FIG. 1.

Sediments of the upper formation immediately beneath the bay bottom have been consolidated under normal load, but deposits in the underlying formation have been preconsolidated. Unconfined compression, water content, and grain-size distribution values were determined on all samples; and Atterberg limits, direct quick shear, and consolidation values were determined on a large propor-

tion of the samples. The shear strength, s, as determined by direct shear tests, was found to approximate closely one-half the unconfined compression, $qu/2$.

Samples were segregated into six groups according to grain size, Group 1 having a range in median diameter between 1 and 2 μ, Group 2, between 2 and 4 μ, and so on, in geometric intervals to Group 6, which ranged between 32 and 64 μ. The strengths of all samples were then plotted against water content for each grain-size group. A definite relationship was found within each group, as illustrated by Fig. 1, which shows the data for Group 4, in which D_{50} ranged between 8 μ and 16 μ. The slopes of the curves for all six grain-size groups varied in a very regular manner. The over-all relationship between strength, water content, and grain size is expressed by the following equation:

$$s = \mathrm{Log}_{10}{}^{-1}\left(\frac{7.5 - 3w - 4\mathrm{Log}_{10}D_{50}}{1.8 - \mathrm{Log}_{10}D_{50}}\right)$$

where s is the shear strength in lb/sq ft, as determined from measurements of unconfined compression, $qu/2$, w is the water content expressed as the ratio of the weight of water to the weight of solid constituents, and D_{50} is the median diameter in microns.

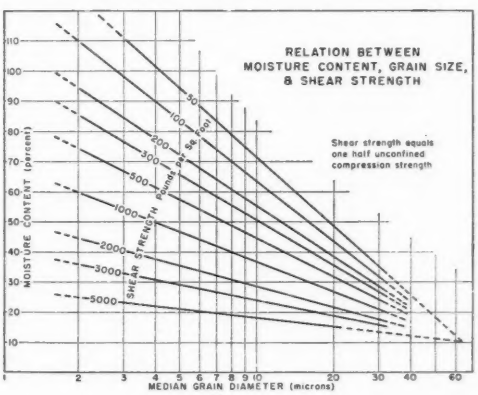

FIG. 2.

The equation is expressed graphically by the family of curves shown in Fig. 2. The reliability of the equation was substantiated by comparing, for 100 random samples, the strength as computed from the equation with the strength as measured in the laboratory. The average observed strength was found to be within 5% of the computed strength. The deviations between observed and computed strength are distributed according to a symmetrical bell-shaped probability curve. The relationship does not hold well for grain size in excess of 32 μ.

Strength naturally is influenced by factors other than water content and grain size. Among these other factors the mineral content, particularly the type of clay minerals, conceivably could be significant. However, in a restricted area such as San Francisco Bay, the newly deposited sediments could be presumed to be relatively similar in mineral and clay composition. This inference is supported by the fact that when the Atterberg limits are plotted on the plasticity chart (*1*), the points lie in a straight and narrow band parallel to and slightly above the "A" line. Apparently, clay and other minerals would have relatively little effect upon the over-all relationships between strength, water content, and grain size in the samples studied.

Factors affecting strength to some extent are mutually interrelated. Water content of sediments varies inversely with grain size (*2*). Also, the plasticity index of the samples from San Francisco Bay varies inversely with grain size. The equation for the relationship is:

$$I_w = 23(2 - \mathrm{Log}_{10}D_{50})$$

where I_w is the plasticity index and D_{50} is the median diameter expressed in microns. Consequently, it follows that in the sediments studied, the three principal variables affecting strength—water content, grain size, and mineral composition—are not completely independent variables.

Further study, particularly of sediments in other areas, is needed in order to appraise the significance of the relationship between strength, water content, and grain size, as observed in sediments of San Francisco Bay. The data obtained thus far, however, indicate that the comparison of unconfined compression with both water content and grain size may give a better understanding of the strength of sediments than comparison with water content alone.

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Interchangeable Pencil-Type Micromanipulator[1]

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The author is engaged in performing operations on the cochlear partition of the inner ear, a working area of less than 1 sq mm. Because the area is so small and speed is so essential in operations on living tissue, most available micromanipulators have proved unsuitable for this work, even though they are quite adequate for anatomical dissection. They are too large and clumsy, require too many complicated adjustments, and do not permit quick interchange of surgical instruments.

An ideal solution would be to have several small, pencil-like micromanipulators, one for each of the necessary surgical instruments. The movements of a handle would be transmitted to the tip, but greatly reduced in magnitude. The carrier for the manipulators should be simple enough to permit quick and easy interchange of manipulators. Thus the instruments could be brought to the

[1] This research was carried out at the Psycho-Acoustic Laboratory, Harvard University, under contract with the U. S. Navy, Office of Naval Research (Contract N5ori-76, Project NR147-201, Report No. PNR-75).

operative field in the same way as ordinary surgical instruments. Such a micromanipulator has been developed with an over-all length of 15 cm and a greatest diam of 2 cm.

Observation of a freehand operation under the microscope reveals two difficulties: (1) it is difficult to bring the instrument into the microscope field, and (2) the involuntary vibrations of the hand can destroy the tissue around the point of operation. The first difficulty can be overcome by having an adequate guide for the manipulator, but the second is much more complicated. Involuntary movements of the point of a pencil held in a comfortable position, with the hand supported by the little finger, while the experimenter tried to keep the tip of the pencil on a given point in the magnified field, amounted to 10^{-2} cm. Even with concentrated attention these vibrations cannot be eliminated (*5*).

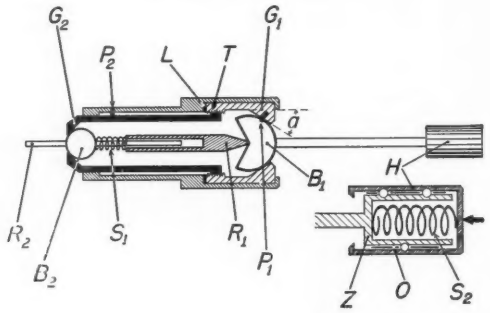

FIG. 1. A schematic cross section of the pencil-type micromanipulator. The tip, on the left, can be moved in three dimensions by moving the handle, on the right. The ratio between the magnitudes of the movements at the handle and at the tip can be set arbitrarily. Insert: Longitudinal shock absorber in the handle of the micromanipulator.

Micromanipulators have been made since the middle of the last century; a summary of such instruments in use today can be found in the handbook of McClung (*4*). The type constructed by Buchthal and Persson (*2*), and Buchthal (*1*) was selected as best suited for modification for the present purposes.

Fig. 1 shows the manipulator described in this paper. It involves a ball, B_1, rotating in a seat. In one side of the ball there is a cone-shaped cavity. The axis of this cone passes through the center of the ball and also through the handle, H, that actuates the ball. The depth of the cone is such that its apex does not quite reach the center of the ball. One end of a rod, R_1, rests in the apex of the cone. The other end of this rod is hollow, and fitted into it is a second rod, R_2, that goes through, and is solidly attached to, a smaller ball, B_2. The free end of R_2 is the tip of the manipulator, to which instruments can be attached. Moving the handle, H, produces movements of the point of the manipulator that are greatly reduced in amplitude. The amount of reduction in the movement from the handle to the tip of the manipulator is determined primarily by the depth of the cone; the closer the apex of the cone to the center of the ball, the smaller the movement of the tip.

In Buchthal's manipulator a special slide was provided to allow movement in the longitudinal direction of the manipulator. In our model the seat assembly G_1 of ball B_1 can be rotated by rotating the handle. This rotation moves the seat assembly G_2 of ball B_2 in the longitudinal direction by means of the threads, T. Ball B_1 has a groove in the plane of the drawing (not shown). A pin, P_1, fits in this groove so that rotation of the ball is transmitted to seat G_1. Thus the seat assembly G_1 can be rotated even when the axis of the handle does not coincide with the axis of the manipulator. A second pin, P_2, moving in a longitudinal groove in seat G_2 prevents a similar rotation of seat G_2. A leather ring, L, eliminates the backlash of seat assembly G_1 in the outside case.

The spring, S_1, has two functions: (1) it eliminates backlash in the threads, T, and (2) it holds balls B_1 and B_2 against their seats. This spring must be strong enough to hold ball B_1 so firmly against its seat that the handle will not fall down of its own weight, but not so strong that it will produce too much friction in the threads. Actually, it was found possible to obtain the required friction in the seat without increasing the friction in the threads by making the angle of the seat of the ball (angle a in Fig. 1) equal to 15 degrees.

For reduction ratios of 10 to 1 or less, the apex of the cone is so far from the center of the ball that the thrust from the spring is strong enough to rotate the ball when the handle is tilted slightly. The action of this spring and ball at these ratios is similar to the action of the ordinary toggle switch, and the handle is stable only at dead center. This condition can be controlled by inserting an auxiliary ring (not shown in the drawing) around ball B_1 inside seat assembly G_1. One side of the ring (toward the right of the drawing) is ground spherically

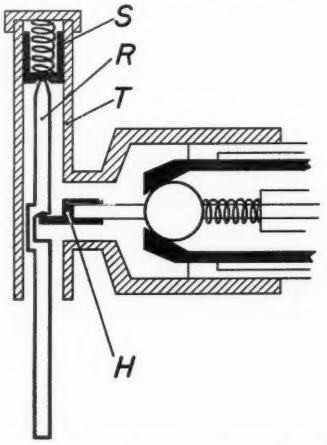

FIG. 2. T-Shaped attachment to change the horizontal type micromanipulator shown in Fig. 1 to a vertical type for operations in deep holes.

to fit the surface of the ball. On the other side of the ring (left) there is a spring that pushes against the beginning of the threads T, holding ball B_1 against its seat. The friction of the ball in its seat will then be great enough to keep the handle H in position. The force of spring S_1 can therefore be reduced and any toggle-switch action eliminated.

When a micromanipulator is used to operate in a small deep hole, difficulties arise with the lever-type manipulator that are not encountered with the slide type. In a slide-type manipulator all the movements are translational and it is possible, therefore, to change the length or angle of the tip without affecting the magnitudes and directions of the displacements in the other axes. Since in the lever-type manipulator the movements are produced by rotations, the linear displacement depends upon the position of the rotating axis.

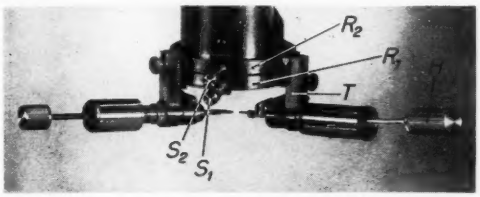

FIG. 3. Mounting for the manipulator on the objective tube of the microscope, eliminating the need for independent coarse adjustments of the manipulator.

The model shown in Fig. 1 was constructed for operations on the surface of the body. This model can be used for operations in narrow holes by adding a T-shaped attachment such as that shown in Fig. 2. To the tip of the manipulator we attach a hook, H, with a small point that fits into a niche in the center of the vertical rod, R. The upper end of the vertical rod rests on the bottom of the piston, S. A spring presses this piston firmly against the tip of the rod. If the hook moves upward, the whole rod is moved upward. A displacement of the hook forward or sideways produces a similar displacement (but one twice as great) of the lower tip of the vertical rod. In this manner movements of the handle H are transmitted undistorted to the lower tip of the vertical rod, where the surgical instruments are attached. The vertical tube, T, of this attachment for operations in a hole has an over-all diam of 4 mm. Consequently it can be placed fairly close to the objective of a microscope without obstructing the field of view.

The lever type of construction is capable of attenuating only the up-and-down and side-to-side vibrations of the hand, as should be obvious from a study of the diagram in Fig. 1. The lengthwise vibrations of the hand are transmitted to the point of the manipulator without attenuation. In addition to these vibrations, the shock produced when the hand touches the manipulator can destroy the preparation. In order to avoid this, it seemed advisable to provide the handle with a shock absorber, as shown in the insert of Fig. 1. A cylinder, Z, is fixed on the end of the handle rod. Two V-shaped grooves are cut on opposite sides of the surface of this cylinder. In the upper groove there are two ball bearings; in the lower, one. They are held in place by the tube, O. A similar pair of grooves is cut in the inner surface of the handle knob, H. A spring, S_2, lightly loads the shock absorber. This shock absorber allows displacement of the handle H along the longitudinal axis, but does not change the transmission of rotation from handle to rod.

The construction of a micromanipulator is complicated by the necessity for coarse, in addition to fine, adjustments. However, since the tip of a manipulator must always be in the field of the microscope during an operation, no provision need be made for these coarse adjustments of the manipulator itself if it can be attached to the microscope tube, as was done by Doty (*3*) and by Tschachotine (*6*). As shown in Fig. 3, a large vertical tube is fixed around the objective of a binocular preparation microscope. On the lower side of this tube are two rings, R, that can be turned easily. Two screws, S_1 and S_2, permit the adjustment of the friction of the rings, R_1 and R_2, relative to the microscope tube. An adjustable carrier for a manipulator is attached to each ring. The manipulators can be turned about their longitudinal axes in the tube, T, of the ring carrier. A pin serves to determine the position of the manipulator. If the angle of the handle, H, relative to the axis of the micromanipulator is kept constant, it is possible to take the manipulator out of the field of the microscope and return it again to exactly the same place. This makes the manipulators easily interchangeable, so that during an operation knives, needles, pipettes, etc., can be used just like ordinary surgical instruments.

For operations such as that on the cochlear partition of the inner ear, a manipulator reduction ratio of 50 to 1 seems to be suitable. Experience with similar operations seems to indicate that fenestration (in otosclerosis of the ear) would be improved by the use of a micromanipulator just as much as it was improved by the introduction of the binocular microscope. Experiments show that in many cases a manipulator with a reduction of 5 to 1 would be very useful.

The micromanipulator described here was constructed in the workshop of the Psycho-Acoustic Laboratory by Ralph Gerbrands.

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An Electron Microscope Study of Isolated Nuclei of Liver Cells from Laboratory Animals[1]

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A study of normal cell components with the electron microscope is an essential preliminary to a study of cytological changes produced by disease. The results of an investigation of isolated nuclei from normal liver cells are given here.

On account of the thickness of whole cells, morphologic studies with the electron microscope can be performed with advantage on isolated cell constituents, although only isolated mitochondria (*5*) and chromosomes (*15*) have been studied so far. Morphologic constituents of the cell have been studied in a variety of other ways with the electron microscope. They have been observed *in situ* in tissue culture cells (*7, 19*), and in tissue sections (*6, 9, 16, 17*). Methods for the fractionation of the fresh cells into its unaltered morphological constituents have been devised and as an approach to the study of the chemical constitution of the cell, Bensley and Hoerr (*2*) have isolated mitochondria and other "large granules." Submicroscopic particulates or "microsomes" were discovered by Claude (*3*) and particulate glycogen was separated by Lazarow (*11*). Nuclei have been segregated by Dounce (*8*), and chromatin threads have been separated by Claude and Potter (*4*). Mirsky and Ris (*13*) isolated chromosomes.

Four mammals—the monkey (*Macaca mulatta*), guinea pig, rat, and mouse—and the 16-day chick embryo of fowl were selected for study and healthy specimens were used. The mammals were all adult. Animals were anesthetized and allowed to bleed in order to eliminate as much blood as possible from the liver. Livers were placed immediately in ice-cooled Petri dishes and were transferred to a cold room (4° C), where the remainder of the process was carried out.

The livers were rinsed with isotonic saline solution and minced with scissors. Buffered hypotonic saline solution, which was 0.6% NaCl buffered to pH 6.2 with phosphates, was used throughout the separation and purification of the nuclei. The centrifugation technique of Dounce (*8*), as modified by Hoerr (*10*), was used for isolating the liver cell nuclei. When the final preparation was obtained, the sediment containing the nuclei was resuspended in a small amount of distilled water and deposited on electron microscope screens, where the drop meniscus was aspirated after 1 min, and the sediment was allowed to dry.

[1] Presented before the annual meeting of the Electron Microscope Society of America, October, 1949, in Washington, D. C.

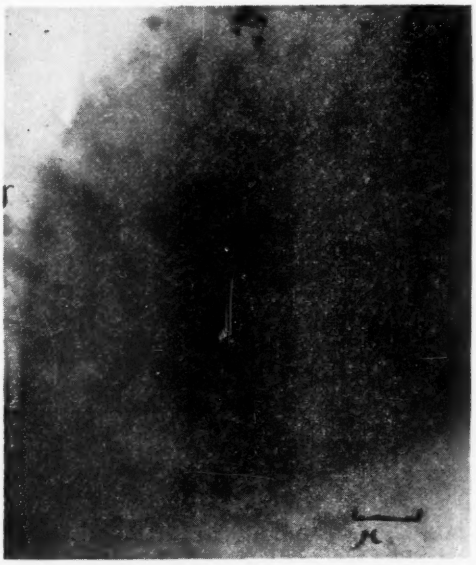

FIG. 1. Isolated nucleus from a monkey liver cell. Unfixed, unstained. Magnification, × 10,000.

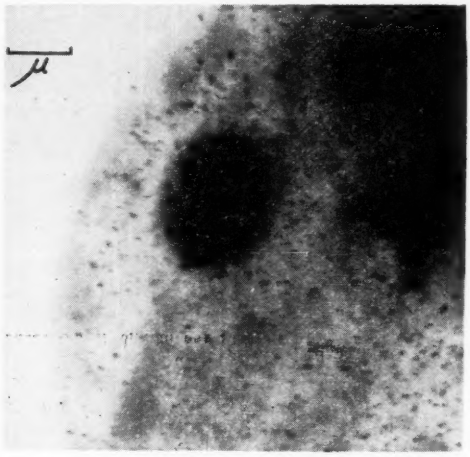

FIG. 2. Isolated nucleus from a monkey liver cell. Unfixed, unstained. Magnification, × 10,000. The nucleus is partly covered by debris.

A few specimens of liver cell nuclei from guinea pig, mouse, and chick embryo were shadow-cast with chromium metal. Image contrast was in general sufficient through the nuclei without shadow-casting, but this process did show up interesting surface morphology not otherwise visible. Original magnifications of a little less than 4,000 times were employed, but in a few cases lower magnifications, around 800 times, were used so that the whole outline of the nuclei would be more readily

observable. An optical microscope was employed for examining control wet preparations with and without staining with 1% methyl green. Smears of the preparation were fixed with methanol and stained with Giemsa's stain for further controls.

In more than twenty isolations of liver cell nuclei from laboratory animals, the shape of the nucleus was preserved and often was almost perfectly oval (Figs. 1, 2), but in most nuclei the nuclear contour was not sharply defined. Many nuclei revealed a coarse network (Figs. 1 and 3), which was indistinct in a few chick embryo nuclei, but easily visible in most of the adult animal nuclei specimens. An identity of this network with the chromatin network observed in the Giemsa-stained con-

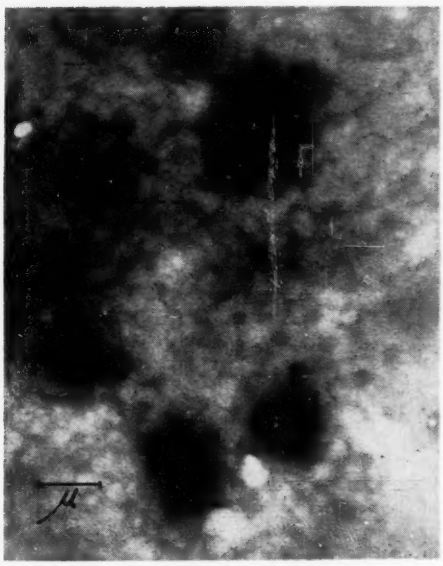

FIG. 3. A portion of an isolated nucleus from a mouse liver cell. Unfixed, unstained. Magnification, × 10,000. To show certain structure in what seem to be nucleoli.

trol smears has not been definitely established, but it is suggested by the close morphologic similarity between them. The nuclei studied here probably have been dehydrated to some extent in the electron microscope, and according to Martens (*12*) and Pischinger (*13*), dehydration reveals the chromatin framework of the nucleus.

Certain dense zones which correspond to structures with enhanced electron-scattering power are seen in all of the nuclei in sharp contrast with the nuclear background. There is no absolute proof that these dense zones correspond to nucleoli, but several observations indicate this. Whenever the word "zone" is used hereafter, it refers to these "dense zones." The number of zones seems to be a function of the animal species from which the nuclei are taken, although in a given species the number may fluctuate slightly at times. Thus, only one zone is noticed in every monkey liver

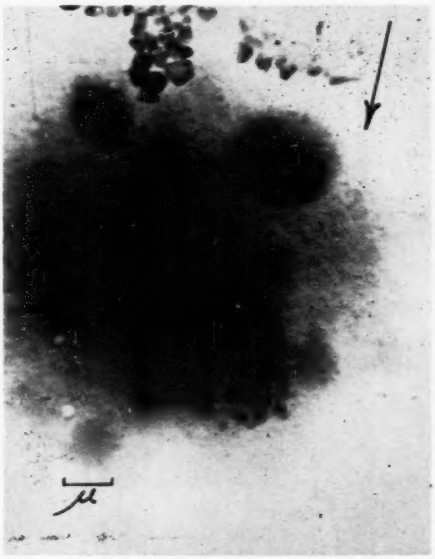

FIG. 4. Isolated nucleus from a guinea pig liver cell. Unfixed, unstained. Shadowed with chromium at an angle whose tangent was 0.24. Magnification, × 8,000.

cell nucleus, two or rarely one in a chick embryo nucleus, and from three to seven in a guinea pig nucleus, although a majority of guinea pig nuclei show four or five each. A number similar to that in a guinea pig nucleus is observed in rat or mouse nuclei.

For a given species the size of the zones varies in the different nuclei, and this difference in size is sometimes quite marked (Figs. 3, 4). However, the zones show an equal density despite their difference in size, so that they must be quite thick, and consequently their shapes are probably either ellipsoidal or spheroidal. No tendency is observed for the zones to occur in definite positions or to be grouped in any repetitive manner within the nucleus, and where there is only one, as in the monkey, it was not seen in a centric position—an observation which points to the identity of zones with nucleoli.

Most of the zones do not show distinct outlines, and although several of them appear homogeneous over their surfaces, others do not. Some have areas of lower density, as well as indefinite and even irregular contours (Fig. 5); the irregular contours are also observed more readily in the shadowed micrographs, as in Fig. 4. This micrograph is a shadow-cast guinea pig nucleus where the shadowing has shown up the fact that the whole nuclear surface is rough, the roughnesses being about 0.1 μ–0.2 μ across. This structure proceeds right across the complete area of the nucleus, including that of the zones, and is apparently a function of the surface of the nucleus as a whole. This, however, is an observation based upon a limited sample. Proceeding as it does over the whole nuclear area, the structure indicates that

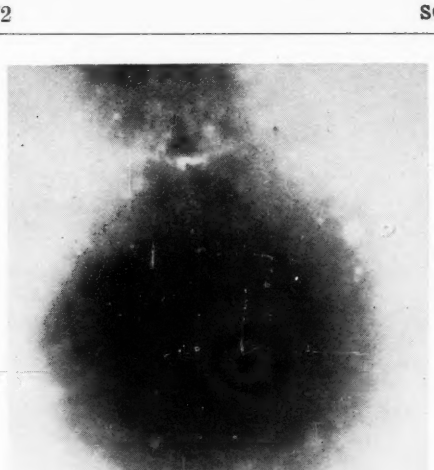

FIG. 5. Isolated liver cell nucleus from a 16-day chicken embryo. Unfixed, unstained. Magnification, × 8,000. This nucleus has apparently suffered plasmolytic changes.

the zones are within the nucleus, not on its surface.

Some of the zones are composed of a dense, oval mass surrounded by two layers: a transparent inner layer and a dense outer layer somewhat thinner than the first (Figs. 2 and 3). This structure has been seen both in monkey nuclei, which show only one zone, and in mouse and guinea pig nuclei, which show several zones per nucleus; it may be revealed in only one zone or in several in a nucleus. The layers are not always visible, and hence this structure may be a function of the preparation. Osmotic action or plasmolysis, or drying during the electron microscope handling may account for the presence of the layers, just as the cell wall of a bacterium is often made visible by these same processes (*14, 20*). In Fig. 3 the outermost layer has a variable thickness ranging from about 600 A to 1200 A. These values are maxima for the observed cases and are either below the resolution of an optical microscope or so close to it that observation of the layers optically would be rather difficult at best.

In the control preparations stained with methyl green, which according to Semmens and Badhuri (*21*) is a specific stain for the nucleolus, deeply stained nucleoli similar in size, shape, position, and number to the zones in the corresponding specimens examined with the electron microscope were seen clearly. Thus, in the optical microscope, only one such nucleolus was observed in preparations obtained from monkey liver; two, or infrequently one, were seen in chick embryo liver specimens, and two to five or even seven corpuscles were noticed in nuclei from guinea pig, rat, and mouse livers. In rat nuclei, there were usually one or two round nucleoli, the rest being either elongated or rather angular. The refringence and affinity for methyl green were the same for all, regardless of their shape or size. In the mouse, the nucleoli in large nuclei were usually larger, but some instances of small ones in large nuclei were noted.

The absence of chemical fixation has not provoked any important distortion in the isolated nuclei examined; rather, all of the morphologic characteristics seem to have been maintained without fixative. This remarkable result is in accordance with the same observation made during a study of chick embryo erythrocytes and reported by us (*1*).

The network of the nucleus observed in unfixed, isolated liver cell nuclei studied here by electron microscopy is morphologically similar to the chromatin framework of Giemsa-stained control nuclei examined with the optical microscope, but it is not similar to the nuclear framework observed in osmic acid-fixed, ultrafine tissue sections examined by electron microscope (*6, 9, 16*).

It may be that the network seen in these electron micrographs of unshadowed nuclei is a manifestation of the pitted nuclear surface visible in shadow-cast specimens. The rims of the pits would indeed appear as a network in the images of unshadowed specimens. Since the observation has been made on a limited sample, it should be confirmed.

The shape, size, and position of the dense zones observed in all nuclei examined, their different electron-scattering power as compared with that of the nuclear background, and the presence of a characteristic number of zones in each animal species examined, all point to an identification of the zones as nucleoli. The nucleoli are known to have a chemical constitution different from that of the remainder of the nucleus. Such differences often result in a difference in electron-scattering power, but since all elements of the nucleus are likely to be light elements, the probability is that the increased scattering power of the zones, as compared with the main body of the nucleus, is due more to an increased physical density. The occurrence of a dense external layer around some of the zones is evidence that some sort of a nucleolar wall may exist, although no nucleolar or nuclear membrane has been detected.

A comparison of the electron micrographs shown here with those obtained from liver sections (*6, 9, 16*) shows that for morphologic studies of the liver cell nucleus unfixed, isolated liver cell nuclei are comparable in electron microscopy with ultrafine, fixed tissue sections, for the present development of both techniques. The isolated nucleus, of course, can be seen in its entirety, whereas the ultrafine tissue sections cannot.

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Blood Findings in Men on a Diet Devoid of Meat and Low in Animal Protein

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During the course of a nutritional survey to be published elsewhere, we became interested in a community of men who do not consume meat and whose animal protein intake is low. Since there is a paucity of data upon the blood findings of humans on prolonged low animal protein intake, it was decided to conduct a blood study of the men in this community.

TABLE 1

PERSONAL HISTORY

Case No.	Age	Age when placed on diet	No. of years on diet	Occupation
1	73	26	47	Woodman
2	62	25	37	Log hauling
3	65	33	32	Cook
4	42	19	23	Gardener
5	44	24	20	Baker
6	36	19	17	Construction
7	37	21	16	Teacher
8	32	17	15	Mechanic
9	48	34	14	Plumber
10	35	23	12	Chauffeur
11	31	19	12	Painter

The 11 men selected for the study had been on the diet from 12 to 47 years, as shown in Table 1. The subjects were never allowed meat, poultry, or fish. The daily animal protein ingested was the milk added to coffee. Since the 1.5 pt of coffee served contained $\frac{1}{8}$ pt of fresh skim milk, the men consumed $\frac{3}{8}$ pt of milk per day. In addition, 5 months of the year, 3 times a week, extra animal protein was consumed in the form of fresh skim milk and American Cheddar cheese; during the remaining 7 months the extra animal protein was consumed once a week for only 17 weeks. During the year, on 28 occasions, the men were served 2 oz of butter at break-

TABLE 2

DIETARY HISTORY

		April 1st–September 13th	September 14th–March 30th
Breakfast*		6 oz whole wheat bread 1.5 pt coffee†	2 oz whole wheat bread 1.5 pt coffee
Noon meal		1.5 pt vegetable soup‡ a vegetable serving§ a fresh fruit serving or 2 oz preserve‖ whole wheat bread ad lib. coffee	1.5 pt vegetable soup a vegetable serving a fresh fruit serving or 2 oz preserve whole wheat bread ad lib. coffee
Evening meal	Sat.	1.5 pt vegetable soup a fresh fruit serving or 2 oz preserve whole wheat bread ad lib. coffee	6 oz whole wheat bread 2 oz preserve 1.5 pt coffee
	Mon.		
	Wed.		
	Fri.		
			17 Sundays
	Sun.	1.5 pt milk 3 in. × 2 in. × $\frac{1}{8}$ in. American Cheddar cheese whole wheat bread ad lib. coffee	1.5 pt milk 3 in. × 2 in. × $\frac{1}{8}$ in. American Cheddar cheese whole wheat bread ad lib. coffee
	Tue.		
	Thurs.		

* On 28 occasions 2 oz of butter was served.

† The coffee was prepared from barley grounds or a mixture of equal parts of barley and soybean grounds. One and one-half pints of coffee contained $\frac{1}{8}$ pint of fresh skim milk.

‡ No meat stock was added to the soup and it was thickened with flour.

§ The vegetable was cooked in water, salt being the only condiment added.

‖ On 28 occasions the fresh fruit or preserve was replaced by a 5-oz piece of plain cake.

TABLE 3

DAILY ANIMAL PROTEIN INTAKE DURING YEAR

No. of days	Foods	Amount in g	Protein* in g
277	Skim milk	177.3	5.7
57	Skim milk	827.5	26.4
	American Cheddar cheese	100.0	24.0
		Total	56.4
28	Skim milk	827.5	26.4
	American Cheddar cheese	100.0	24.0
	Butter	56.2	0.56
	Egg	14.3	1.85
		Total	52.81

* The values for the protein content of the foods were taken from the Tables in *Nutrition in health and diseases* by Cooper, Barber, and Mitchell (*1*).

TABLE 4

HEMATOLOGICAL AND CHEMICAL FINDINGS

Case No.	Hematocrit	Hemoglobin	Red blood cells*	White blood cells†	Differential count of white blood cells: Polymorphonucleurs	Lymphocytes	Monocytes	Eosinophils	Basophils	Chemical findings: Iron	Glucose	Nonprotein nitrogen	Total serum protein	Serum albumin	Serum globulin
	%	g/100 ml			%	%	%	%	%	mg‡	mg	mg	mg	mg	mg
1	46.0	15.0	5.30	8.9	57	36	0	7	0	50.36	112.9	31.6	6.0	4.1	1.9
2	41.2	14.15	4.98	7.9	63	32	2	3	0	46.91	113.1	29.5	7.5	4.9	2.5
3	50.0	15.61	5.81	6.7	66	30	1	3	0	51.76	123.7	32.8	6.3	4.2	2.1
4	38.8	13.41	4.49	8.2	62	35	3	0	0	45.79	...	25.2	6.9	4.9	2.0
5	46.1	15.33	5.33	7.5	54	41	2	2	1	51.40	85.8	33.6	7.5	4.8	2.7
6	49.5	16.51	5.98	8.4	61	34	2	3	0	53.51	108.1	38.3	6.1	4.1	2.0
7	...	...	...	...	67	29	1	2	1	...	...	25.4	7.2	4.8	2.4
8	47.0	15.53	5.54	8.1	59	33	6	2	0	51.93	90.6	36.2	6.7	4.7	2.0
9	45.0	15.40	5.26	8.5	51	45	1	2	1	52.14	...	37.2	7.7	5.2	2.5
10	45.0	14.97	5.11	6.8	61	34	2	3	0	50.19	101.1	26.5	6.3	4.0	2.3
11	43.2	15.22	5.19	6.5	62	35	1	2	0	51.03	...	...	...	...	...

* Millions per cu mm.
† Thousands per cu mm.
‡ Chemical findings are expressed in mg/100 ml blood.

fast and 5 oz of plain cake, prepared with eggs and milk, at the noon meal. The menu as shown in Table 2 was never varied except for the kind of vegetable, fruit, or preserve served. Thus, the total yearly animal protein intake was that contained in 8 eggs as calculated from the plain cake recipe, 56 oz of butter, 259 pt of milk, and 286.2 oz of American Cheddar cheese. The National Research Council's recommended daily protein allowance is 70 g, of which half, or 35 g, should preferably be of animal origin. In this study, the daily animal protein intake, as shown in Table 3, for 277 days, 57 days, and 28 days of the year was 5.7 g, 50.4 g, and 52.8 g, respectively.

Venous blood was withdrawn from the subjects. Hematocrit, hemoglobin, red cell count, white cell count, iron, sugar, and nonprotein nitrogen determinations were made on the oxalated sample; total protein, albumin, and globulin determinations were made on the blood serum; differential counts were done on blood smears. Results of blood studies are summarized in Table 4.

Despite the fact that the subjects had been on a diet devoid of meat and low in animal protein for at least 12 years, and in one case for 47 years, the blood findings fall within the normal range. These findings are in contrast to the findings of Hegsted *et al.* (*2*) and of Kark *et al.* (*3*), who have reported a correlation between the protein intake and serum concentration, but are in keeping with the work of Youmans *et al.* (*4*), who reported no demonstrable correlation between intake and serum levels. Since the low animal protein intake was not reflected in the blood determinations performed, it appears that either (1) the National Research Council's recommended requirement is too high; (2) vegetable protein combinations can be substituted for animal protein; or (3) chemical determinations other than those performed might reflect the low intake. At present this laboratory is engaged in animal experiments to investigate the second and third premises.

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Comments and Communications

Biologists in Military Service

The recent article by Wigodsky (*Science*, 1949, **110**, 135) is a challenge calling for study and action. He charges that the military services are dealing inadequately with "the problem of science" and that organized science is insufficiently interested in the actions of the military services—"With the exception of certain of the civilians on the Research and Development Board, . . . none of the top rank positions within the three armed services is held by an outstanding scientist."

Wigodsky does not clearly restrict his discussion to scientists in uniform. His quotations from *Scientists in Uniform, World War II*, a booklet published by the Army, imply such a restriction, but on the other hand he emphasizes the role played by civilians holding appointments on the RDB. Since scientific societies have not advocated that all scientists in the armed forces be in uniform, it will be assumed that Wigodsky has an open mind on that subject.

I do not speak officially for the Department of Defense, the Department of the Army, or the Chemical Corps. My views are my own, based on experience as a biological scientist working for eight of the past nine years in and out of uniform for the armed forces, including the Air Force, the Quartermaster Corps, and the Chemical Corps. As a councillor of the American Physiological Society for the past three and a half years I have participated in many discussions of the position of scientists in government laboratories.

The example of the Medical Division, Army Chemical Corps, can be cited as evidence that the problem of scientists and the armed forces can be solved in peacetime. The senior scientists in the Medical Division during the war were on leave from their civilian posts, at considerable inconvenience and often financial sacrifice. They conceived it their duty to serve as officers in this research laboratory. Once the war was over, there was a quick exodus; there was a general feeling that their own interests and the country's peacetime interests would be served best by their return to prewar posts.

At this stage the wisdom of the chief of the Medical Division, Col. John R. Wood, M.C., was demonstrated. Col. Wood had been selected by the Army Medical Department for assignment to this position in the Chemical Corps. He foresaw the impossibility of staffing a research laboratory in the postwar era with scientists in uniform. He drew up an organizational chart with three research branches and an administrative branch. The former branches and the constituent sections were to be headed by civil service appointees; the latter branch by an officer. About seven-eighths of all the positions were civilian. The other places were to be filled by regular and reserve officers, most of whom were to be trained for a research career. This plan was approved by all concerned; steps were then taken to implement it. The three principal steps were to appoint recognized biologists to responsible positions, to insure maximum stability, and to provide for the training of officers. Progress was slow but encouraging; now that the goal established in 1945 has been achieved, it is time to take stock. Evidence that the first step succeeded is seen in the recognition given to the senior staff. Seventeen of them hold membership in one or more of six societies that form the Federation of American Societies for Experimental Biology.

There are many facets to building a research organization having stability and high morale. Evidence of both is found in the rate of turnover. For the Medical Division as a whole there were thirty separations for all causes during the year ending June 30, 1949. This is about 15% of the present staff. Only two of the senior biologists left, one to industry and one to a university, both having had offers which could not be met. One of the major requirements is that research workers be enabled to carry on independent research that can be published. The Chemical Corps is on record (*Symposium on military physiology*. The National Military Establishment, Res. and Dev. Board, Digest Series No. 4, 1947. GE 61/1, pp. 9–10.) as follows:

> Competent scientists are wedded to fundamental research, and fundamental research is vital to the success of a research and development organization.
>
> Our scientists of Ph.D. caliber are encouraged to undertake original independent research within the broad field of Chemical Corps responsibilities. They are not placed under the onus of producing within six months or a year applicable results from such research. It is assumed that this policy will bear fruit in the form of fundamental discoveries of great importance to science; it is hoped and believed that some of these discoveries eventually can be applied by our engineers. In any case, it is certain that these scientists will grow in stature and will be strengthened in their loyalty to the Chemical Corps by this policy.

Evidence that opportunities for research exist in the Medical Division and among contractors is found in the record of work published. During the year ending June 30, 1949, the Medical Division staff published 54 papers, while university investigators supported by the Medical Division published 37 papers.

Stability in a research organization requires opportunity for professional advancement. This includes not only freedom to publish but also interchange of ideas with leaders in research. Such an interchange is provided by having distinguished scientists lead weekly seminar discussions, by occasional visits from consultants who are eminent in the various medical sciences, by visits to research institutions, by encouraging attendance at scientific meetings, and by an organized graduate training program. It is hoped to pay the expenses of each scientist to one meeting per year if he has a paper to present. Graduate training leading to degrees is provided through a contractual arrangement with the University of Maryland. Courses in many of the medical sciences are given at Medical Division, and opportunities are offered for research. Instructors are chiefly scien-

tists on the Medical Division staff who are given appointments on the faculty of the University of Maryland for this purpose. Those who participate are allowed by civil service regulations to spend one-tenth of the 40-hour week taking such courses. Our laboratories are opened after hours where needed.

The relation between the military and the civilian appeared to be of major concern to some of the respondents reported in *Scientists in Uniform.* No serious problem of this nature has arisen in the Medical Division. This is due in part to the characteristics of the people involved; it is also due to the fact that, with few exceptions, officers and civilians have different functions and are not competitive. At any rate, our experience proves that the relations between officers and civilians can be harmonious in a research laboratory of the armed forces.

Training of officers. There are now 34 officers in the Medical Division, the majority of whom belong to the Chemical Corps. All have had some interest and qualifications in the biological or allied sciences. None are kept on except those who demonstrate professional ability. An officer trained in this way for two or three years is not necessarily lost to the Medical Division. If he proves gifted in research, he may return for subsequent tours of duty. If war comes again and necessitates an increase in staff, he may be brought back as an officer or a civilian, whichever seems appropriate. Chemical Corps officers trained here may well reach positions of authority in another ten years.

These steps have not been taken easily. There are minor sources of irritation which rankle with some and are taken in stride by others. Regular fixed hours of work are anathema in academic circles, but seem unavoidable in civil service. The formality of making a new appointment is matched only by the difficulty of uprooting an unsatisfactory "permanent" employee. "Clearance" has been slow and has involved procedures abhorrent to scientists.[1] It is only fair to say, however, that in no instance during the past year has any employee, prospective or on the job, been lost because of clearance troubles. Usually an interim clearance can be obtained.

In peace or war, there seems to me to be no essential difference between the scientist in uniform and the same scientist employed as a civil servant. In wartime laboratories scientists in and out of uniform worked side by side. Early in the war there were administrative difficulties when civilian scientists went to theaters of operation; these were partly removed when a uniform and "simulated" rank were authorized. It is true that 80% of the biologists covered by *Scientists in Uniform* thought that better methods of assignment and of supervision were needed. This does not imply that 80% were dissatisfied; actually 45% of the 2,830 reporting were utilized in their own or in collateral fields. Perhaps the basic error was made in putting so many biologists in uniform. Three pertinent questions should be resolved before another war comes: How many biologists are needed in the armed forces? How many of them should be in uniform? How can the others be persuaded to remain in their own laboratories?

Wigodsky urges that the relation of scientists to the armed forces be studied by a committee of biologists. This recommendation, insofar as it concerns physiologists, was considered by the Council of the American Physiological Society at its recent Augusta meeting. The council concluded that the American Institute of Biological Sciences (of which the Physiological Society is a member) is best qualified to deal with the matter. Furthermore, it was considered that the area covered should be greater, and it was recommended: "That the scope of the Institute's Committee Advisory to the Armed Forces be extended and broadened to include the utilization of all biologists in Government services." This committee, which represents a large number of professional biologists and which is also under the wing of the National Research Council, should be competent to deal with Wigodsky's questions as well as subsidiary questions raised above.

If such action is taken by the AIBS, a logical question will be: How many biologists are there in government service? While no complete answer can be given to this question, the directory of the Federation of American Societies for Experimental Biology (*Fed. Proc.*, 1949, **7, 8,** 667) lists the affiliations of members of its component six societies. This directory shows 43 members in the Department of Agriculture, 14 in the Atomic Energy Commission, 3 in the Civil Aeronautics Authority, 13 in the Air Force, 53 in the Army, 11 in the Navy, 18 in the Food and Drug Administration, 65 in the National Institutes of Health, 11 in other departments of the Federal Security Agency, and 17 in the Veterans Administration—a total of 248. This is a fair approximation of the distribution of senior biologists (in the six fields concerned) in federal service. Many large groups of biologists are not in the federation; e.g., bacteriologists, geneticists, plant physiologists, zoologists, and entomologists.

It is hoped that this AIBS committee will consider means for strengthening the bonds between scientists in and out of government laboratories, without regard to the question of uniform. For example, can these bonds be strengthened by relying on the government's scientists for advice in placing research contracts? This has proved a fruitful arrangement; contracts are entered into only after consultation between Medical Division scientists best qualified in the field and the university scientists who are to conduct the research. This arrangement is designed not to interfere in any way with the conduct of the university scientist's research program. Rather, it provides mutually valuable opportunities for exchange of visits and ideas.

DAVID B. DILL

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[1] This subject has been dealt with admirably by Lee A. DuBridge in the *Atlantic Monthly,* October, 1949.

Fluorescence of Amino Acids

In the December 2, 1949, issue of *Science*, A. R. Patton, Elsie M. Foreman, and Patricia C. Wilson published observations which led them to the conclusion that fluorescence by dry amino acids is "an assumption which appears unwarranted."

While we are in agreement with their observations gained with glass plates and filter paper, we wish to point out some differences of interpretation of the results. Even if one is to disregard J. de Ment's report on fluorescence of amino acids in the solid state observed at wavelengths 3650 A–3600 A (de Ment, A. and Dake, *Ultraviolet light and its application.* New York: Chemical Publishing Co., 1942.) One has to contend that more than a simple browning reaction between the amino acids and the paper is involved. Many organic substances display similar browning after prolonged heating of the paper. Assuming that it is a Maillard (browning) reaction, it must be one between the amino group of the amino acid and the paper, which results in no critical change in the amino acid molecule, as the subsequent ninhydrin reaction is strongly positive. Moreover, it has been observed that N-substituted amino acids do not fluoresce (Platner and Nager. *Helv. Chim. Acta*, 1948, **31**, 2203; Gal and Greenberg. *Proc. Soc. exp. Biol. Med.*, 1949, **71**, 88). The reasoning that extraction of the amino acid does not affect the fluorescence of the spot can be countered by the fact that neither the amino acids nor the pyrimidines or purines are 100% extractable from the paper; the losses amount to 7%–9%. This can easily be checked by radioactively labeled material. The nonextractable material might possibly be amino acids that have undergone an advanced browning reaction to the point of cyclization. In any case, in our experience, some amino pterines, and even ammonium hydroxide (prepared from ammonia gas and distilled water) leave similar fluorescent spots behind on the paper. This relationship becomes more complicated if the effect of solvents is taken into consideration. Whether this effect can be so simply described as a *sine qua non* of the filter paper is still an open question.

Another possibility is the physical aspect. It is a well-known fact that many substances that show no fluorescence in the solid state or in solution produce emission when brought into contact with a finely porous insulator, such as cellulose, cotton, or fine aluminum oxide. The insulation assures adequate isolation of radiating molecules from their neighbors so that the excitational energy cannot be dissipated. This is interpreted to mean that the main part of the substance cannot absorb energy from the activated particles, whose concentration remains at an optimum, sufficient to fluoresce. However, this possibility remains to be tested in the case of amino acid adsorption.

EMERY M. GAL

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The Use of a Fathometer for Surveying Shellfish Areas[1]

Although echo or sonic sounding instruments were designed primarily for navigational purposes, some of them have proved useful for hydrographic surveys and to locate schools of fish (Adams, K. T. *Hydrographic Manual*, U. S. Coast and Geodetic Survey Spec. Pub. #143, 1942; and Tester, A. L. *Bull. Fish. Res. Bd.*, Can. LXIII, 1943).

A portable depth recording instrument, Model 808-J, manufactured by the Submarine Signal Company, was recently used to obtain profiles of Pamlico Sound, North Carolina, in a survey of the bottom for shellfish beds. Several transects were made between the major shoals of the sound in depths of water varying from 10 ft to 25 ft. The different intensities of the recordings, indicating hard or soft bottom, were checked with a leadline and material was dredged with a conventional oyster dredge. In general, when hard bottom rising a few feet above the surrounding mud was located, it was found to be an oyster bed. From some fathograms it was possible to distinguish shell bottom from hard sand, although scattered oysters lying on hard sand bottom were not readily distinguishable.

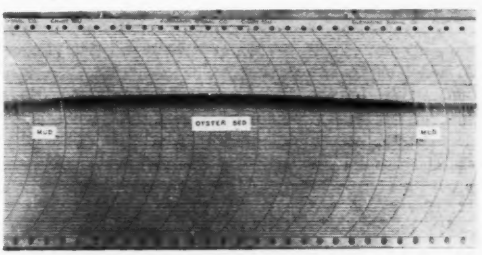

FIG. 1.

Fig. 1 is a photograph of a recording obtained while passing over an oyster bed. The depth of water overlying the bed is indicated in feet by the horizontal lines along the vertical scale A.

A. F. CHESTNUT

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[1] The Institute of Fisheries Research is indebted to the Submarine Signal Company of Boston, Massachusetts, for the loan of the fathometer.

The Chalkley Equation for Volume-Surface Ratios Applied to Open Figures

With reference to the excellent paper by Chalkley, Cornfield, and Park on the estimation of volume-surface ratios of closed three-dimensional figures (*Science*, 1949, **110**, 295), I should like to point out that the figures need not enclose finite volumes and that therefore the method has a somewhat broader field of application than the authors have indicated.

To show this, let V_x represent the volume enclosed by a surface of area S_x, which itself is contained in a substance y of volume V_y, and let h_x and h_y represent the hits recorded in V_x and V_y respectively. The equation developed by Chalkley *et al.* is then $V_x/S_x = rh_x/4c$, in which r is the length of the needle or test line and c is the number of cuts recorded. But $V_x/V_y = h_x/h_y$. Hence $V_y/S_x = rh_xh_y/4h_xc = rh_y/4c$, which is the ratio of the volume of y to its internal surface area. Obviously, V_x and hence h_x may approach arbitrarily close to zero, so that this expression is valid for finite surfaces enclosing infinitesimal or zero volumes. This being true, the expression is also valid for open three-dimensional figures.

An example of a case to which this equation might be applied is the determination of the internal surface area of an incipiently fractured material by means of measurements on random polished sections.

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The Structure of the Acropeptides

In the 1949 edition of R. A. Gortner and W. A. Gortner's *Outlines of Biochemistry* (New York: John Wiley & Sons, 1949) reference is made on page 366 to our work on the nature of the acropeptides, viz., the products of the nonhydrolytic breakdown of various proteins (Fodor, A. and Kuk, S. *Biochem. Z.*, 1931, **240**, 123; 1932, **245**, 350). Our claim that they are closed polypeptide rings with neither *terminal* amino nor carboxyl groups is reported to have been disproved by T. S. Reid (Ph.D. thesis, Univ. of Minnesota, 1943), who insists that they are products of an alcoholysis brought about by resorcinol. We therefore wish to state the following facts:

(1) We have noticed that heating proteins in media such as ß-naphthol or resorcinol results in products which contain as a maximum 2% of these substances. Use of these media was therefore abandoned in favor of dry glycerol.

(2) We were able to prove the ring structure of the acropeptides by means of a simple calculation, based on experimental data: The number of the hexone bases—histidine, arginine, and lysine—was estimated quantitatively in acropeptides from casein. Each of these amino acids possesses, in addition to the α-carboxyl amino group which partakes in the peptide linkages and therefore cannot be estimated by titration, one more group of amino or imino nitrogen which *is* titrable by Linderstrom-Lang's titration method. The various fractions obtained from the crude breakdown product, however, gave a considerable titer in acetone, which equaled exactly the sum total of the number of (amino + imino)-nitrogen groups located in the side chains of histidine (imidazolyl ring), arginine (guanidino group), and lysine (ε-amino group) estimated quantitatively. This, in our opinion, is the most conclusive evidence for the absence of either terminal amino or imino groups in those products. If strictly nonhydrolytic conditions were observed the lowest molecular weights of our various fractions were never below 900 (Fodor, A., Fodor, P. J., and Kuk-Meiri, S. *Enzymologia*, 1947, **12**, 101).

(3) It cannot be discussed here whether the acropeptides are already preformed in the proteins or whether they are formed in the process of heating by virtue of the existence of juxtaposed carboxyl and α-amino groups, a possibility which has been envisaged before (Fodor, A. *Enzymologia*, 1939, **6**, 207). It should be mentioned in this respect only that enzymatically their behavior is in good agreement with what is known today on the correlation between the occurrence of certain amino acid residues in proteins and synthetic peptides and the specific action of proteinases.

(4) The review in Gortner's book on protein structure refers in general to the more recent publications but those of our papers that he mentions date back to 1936, although we made a comprehensive report as late as 1947, which we have already cited.

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The Conversion of Phosphorylase A to Phosphorylase B by Blood Tryptase

Cori and Green (Cori, G. T. and Green, H. A. *J. biol. Chem.*, 1943, **151**, 31) have shown that the proteolytic enzyme found in muscle and spleen converts phosphorylase A to phosphorylase B. They observed also that trypsin, acting at pH 6.0–6.2 brings about this change. I have demonstrated that the blood protease known as "tryptase" and also called "plasmin" and "fibrinolysin" (Ferguson, J. H. *Science*, 1947, **105**, 488) forms phosphorylase B from phosphorylase A. I have made quantitative determinations of phosphorylase A according to Cori and Cori and Green (*J. biol. Chem.*, 1943, **151**) and of phosphorylase B after addition of adenylic acid. The tryptase was a lyophilized preparation obtained from the Parke, Davis and Company.

It is already known that both plant and animal substances can inhibit tryptase (Christensen, L. R. and MacLeod, C. M. *J. gen. Physiol.*, 1945, **28**, 559; Mirsky, I. A. *Science*, 1944, **100**, 198) and I have found that soybean antitrypsin is very effective in preventing tryptase from converting phosphorylase A into phosphorylase B. Glycogen also inhibits this tryptase action but not completely.

I wish to thank Prof. James B. Sumner for his interest in this problem, and the Rockefeller Foundation for financial assistance.

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Association Affairs

Meeting of the Southwestern Division of the AAAS

Flagstaff and Grand Canyon, Arizona, provided the locale for the 26th annual meeting of the Southwestern Division of the American Association for the Advancement of Science, April 30–May 4. Arizona State College, Lowell Observatory, and the Museum of Northern Arizona were host institutions at Flagstaff; and most of the 150 scientists and students who attended the sessions also journeyed the 105 miles to the South Rim of Grand Canyon to participate in a dinner at El Tovar, and to hear the John Wesley Powell Memorial Lecture by Edwin D. McKee. Short field and inspection trips on the canyon rim, scheduled for May 4, were somewhat handicapped by fresh snow, but snow and a temperature in the mid-twenties failed to chill the enthusiasm that pervaded the meetings.

Of 89 papers listed in the program, 43 dealt with biological subjects, 29 with physical science, and 17 with the social sciences. In the biological field emphasis naturally fell upon Southwestern faunas and floras, but subjects of more general interest were by no means neglected. Two papers on antibiotics, several on physiological functions in man and beast, and an entire session devoted to plant pathology demonstrated that Southwestern biology does not suffer from provincialism, even though the special adjustments of plants and animals to the varied environments of the region would tempt any scientist to devote himself to local natural history. The African snail was featured as a major economic menace in the Pacific, not only in a sectional meeting, but also in a general lecture on Micronesia by Albert R. Mead.

The Physical Sciences Section arranged symposia in the fields of subatomic phenomena, pure chemistry, meteorites, and astronomy. In the symposium on subatomic phenomena, M. H. Wilkening, of the New Mexico School of Mines, described procedures for the determination of radioactivity in the atmosphere caused by the adsorption of the disintegration products of radon on dust particles. The experimental results show that there are approximately 1500 alpha disintegrations per minute per cubic meter due to radon in the atmosphere. F. E. E. Germann and co-workers from the University of Colorado presented the results of experiments on the fluorescence of uranyl platinocyanides. Theodore G. Klose, of Arizona State College at Tempe, reported on the structure of synthetic musks, proving that Musk Ketone and Musk Tibetene are 4-t-butyl-2,6-dimethyl-3,5-dinitroacetophenon and 5-t-butyl-3,5-dinitrohemimellitene, respectively.

A new approach in estimating the mass of the meteorite that caused the Canyon Diablo crater was reported by Lincoln La Paz, of the University of New Mexico, who postulates that the meteorite must have had a mass of approximately 1,000,000 tons for it to have formed a crater 2,000 feet in diameter and 500 feet deep. H. H. Nininger, director of the American Meteorite Museum, Winslow, Arizona, discussed the use of the Knoop indenter technique on small fragments of the Canyon Diablo meteorite. Members of the staff from the Lowell Observatory of Flagstaff, Arizona, presented a series of papers on planetary atmospheres, and C. O. Lampland discussed a project on a new determination of the planet Pluto.

The Social Sciences Section's three technical sessions were concerned with recent archaeological discoveries in the Southwest, Indian culture, and analyses of social attitudes.

Following the Division's annual dinner, Oscar B. Muench, of New Mexico Highlands University, in his retiring presidential address discussed "Radioactivity and Its Relation to the Determination of Geologic Age" (to be published in an early issue of *The Scientific Monthly*). C. W. Botkin, of New Mexico A&M College,

Arthur Adel Oscar Muench C. W. Botkin Fred Emerson Jesse A. Hancock

NEW OFFICERS AND COUNCIL MEMBERS, SOUTHWESTERN DIVISION, AAAS

was elected to succeed Dr. Muench as president for 1950–51; Fred Emerson, of New Mexico Highlands University, succeeds H. H. Nininger as vice president. Arthur Adel, of Arizona State College, and Jesse A. Hancock, of Texas Western College, were elected to the Executive Committee. The Colorado delegation, headed by Frank E. E. Germann, secretary of the Division, announced regretfully that facilities at the University of Colorado will not be ready for use in the spring of 1951; hence, it was voted to hold the next meeting in El Paso, April 29–May 3, with Texas Western College as host.

HOWARD MEYERHOFF

Administrative Secretary

Program of Section G-Botanical Sciences, AAAS Cleveland Meeting, December 26–30

Arrangements have been completed for two of the symposia planned by Section G for the 117th Meeting of the American Association for the Advancement of Science in Cleveland this December. These are:

I. *The Ecological Background of Evolution.* One session, Friday morning, December 29. Speakers include Herbert P. Riley, University of Kentucky; G. Ledyard Stebbins, Jr., University of California; Pierre Dansereau, University of Michigan; Colin Pittendrigh, Princeton University; Edgar Anderson, Missouri Botanical Garden; and David D. Keck, New York Botanical Garden. Titles will be announced at a later date. This symposium will also be of particular interest to the biological and zoological societies meeting with the Association.

II. *The Structure and Analysis of Plant Communities.* Two sessions, Saturday morning and afternoon, December 30. Speakers include Stanley A. Cain, Cranbrook Institute of Science; Francis C. Evans, University of Michigan; George W. Thomson, Ethyl Corporation; Lee R. Dice, University of Michigan; John T. Curtis, University of Wisconsin; and Grant Cottam, University of Wisconsin. Titles will be announced at a later date. This symposium will also be of particular interest to the members of the Biometric Society, Eastern North American Region, especially since it follows the six-session symposium on mathematical biology and biometry which this society is planning.

As announced in *Science* (May 12, p. 528), Section G will also hold sessions for contributed papers during the first part of the Association's meeting. For purposes of session room scheduling, tentative titles and subject classifications should be sent to the Secretary of Section G *as soon as possible.* Final titles may be submitted as late as *September 15.*

STANLEY A. CAIN, SECRETARY

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Scientific Book Register

Medical Physics, Volume II. Otto Glasser, Ed. Chicago, Ill.: Year Book Publ., 1950. 1227 pp. $25.00.

The Ants of North America. William Steel Creighton. Cambridge, Mass.: Museum of Comparative Zoology, Harvard College, 1950. 585 pp. and 57 plates.

The Foundations of Arithmetic: A Logico-Mathematical Enquiry into the Concept of Number or "Die Grundlagen der Arithmetik." Gottlob Frege; English trans. by J. L. Austin. Breslau: Verlag von Wilhelm Koebner, 1884; New York: Philosophical Library, 1950. 119 pp. German and English text. $4.75.

General Chemistry for Colleges. Jelks Barksdale. New York-London: Longmans, Green, 1950. 504 pp. $5.00.

First Principles of Atomic Physics. Richard F. Humphreys and Robert Beringer. New York: Harper, 1950. 390 pp. $4.50.

Mercury Arcs. 2nd ed. F. J. Teago and J. F. Gill. London: Methuen and Company; New York: John Wiley, 1949. 107 pp. $1.50.

Infrared Radiation Therapy Sources and Their Analysis with Scanner. Leopold Rovner. Springfield, Ill.: Charles C. Thomas, 1950. 34 pp. $1.50.

The Psychology of Exceptional Children. Rev. ed. Karl C. Garrison. New York: Ronald Press, 1950. 517 pp.

A Systematic Laboratory Course in General Chemistry. Harry H. Sisler and Jay J. Stewart. New York: Macmillan, 1950. 396 pp. $3.00.

The Christian Response to the Atomic Crisis. Edward LeRoy Long, Jr. Philadelphia 7: Westminster Press, 1950. 112 pp. $2.00.

Human Ecology: A Theory of Community Structure. Amos H. Hawley. New York: Ronald Press, 1950. 456 pp. $5.00.

X-Ray Optics: The Diffraction of X-Rays by Finite and Imperfect Crystals. A. J. C. Wilson. London: Methuen and Company; New York: John Wiley, 1949. 127 pp. $1.50.

Vector and Tensor Analysis. Harry Lass. New York-London: McGraw-Hill, 1950. 347 pp. $4.50.

The Use of Chemical Tests for Alcohol in Traffic Law Enforcement. Glenn C. Forrester. Springfield, Ill.: Charles C. Thomas, 1950. 91 pp. $2.00.

An Introduction to the Laplace Transformation. J. C. Jaeger. London: Methuen and Company; New York: John Wiley, 1949. 132 pp. $1.50.

Atoms of Thought: An Anthology of Thoughts from George Santayana. Ira D. Cardiff, Ed. New York: Philosophical Library, 1950. 284 pp. $5.00.

NEWS and Notes

Edwin G. Conklin, professor emeritus in biology at Princeton University, has retired from the Academy of Natural Sciences of Philadelphia, after serving 50 years as vice president and 13 years as trustee.

Gottfried S. Fraenkel, of the Entomology Department, University of Illinois, is spending three months in Hawaii, organizing research on the physiology of the oriental fruit fly for the U. S. Department of Agriculture. **Clifford C. Roan,** graduate assistant on the university staff, will be in permanent charge of the research, in which the State of California is cooperating. Headquarters for the project will be at the University of Hawaii.

Webster P. True, chief of the Editorial Division, Smithsonian Institution, for the past ten years, retired on May 31. Dr. True came to the Smithsonian as an editorial clerk in 1914. **Paul H. Oehsor,** assistant chief of the division, has been appointed to take his place.

Armand N. Spitz, director of education at the Franklin Institute, has been elected chairman of the Science Museum Section of the American Association of Museums. Dr. Spitz will be in charge of the coordination of U. S. science museum activities and the development of joint activities on a national basis.

Stanford Research Institute has appointed **Rodolfo Hernandez Corzo,** director of the National School of Biological Sciences, Mexico City, as its first international research fellow. Mr. Corzo will spend two years at the institute and at Stanford University in advanced work in genetics, radiochemistry, and microbiology.

Ralph A. Bradley, of McGill University, Montreal, and **David Duncan,** recent lecturer at the University of Sydney, Australia, are new associate professors in the Department of Statistics, Virginia Polytechnic Institute. Dr. Bradley will conduct research on rank order statistics.

Ernest Carroll Faust, head of the Division of Parasitology at Tulane University's School of Medicine, will spend a month this summer at the University of Santiago, Chile, as visiting professor. In August he will attend the Fifth International Congress of Microbiology, in Rio de Janeiro, as official delegate of the university and the American Academy of Tropical Medicine.

Visitors to U. S.

D. A. Walsh, of Leeds University, England, will be a visiting lecturer in the School of Chemistry at the University of California at Berkeley during the fall semester.

Hideo Kunabe, general manager of the Antituberculosis Association of Japan, and **Tomio Ogata,** editor of the *Journal of the Japanese Medical Association* and professor of serology at the University of Tokyo Medical School, are in the U. S. for a 90-day training program under a fellowship plan established by the Military Government of Japan. Dr. Kunabe is studying tuberculosis control and clinical and research programs. Dr. Ogata is studying production of medical and health journals and the use of medical exhibits and visual aids.

Richard Kuhn, director of the Max Planck Institute for Medical Research, Heidelberg, Germany, lectured June 5 and 6 at the National Institutes of Health, Bethesda, Maryland.

Walter Roos, engineer and works manager, and **G. A. Schroter,** chemist, both of the Feldmuhle Papier u. Zellstoffwerke, Wesseling bei Köln, Germany, and **P. Cornaud,** professor at the University of Ghent, visited the National Bureau of Standards recently.

Grants and Awards

The vice chancellors of the Universities of Denmark have made the first award of the **Augustinus Prize** to Bengt Strömgren, director of the University Observatory of Copenhagen, for his accomplishments in astronomy and astrophysics. The prize, recently established by the Augustinus Industries of Denmark, consists of an award of 50,000 Danish crowns—$5,000 at the current rate of exchange.

The $2,500 Merck Graduate Fellowship in Analytical Chemistry for 1949 has been awarded to John T. Byrne, teaching fellow and research assistant at the Massachusetts Institute of Technology. The fellowship, established in 1948, goes to the applicant considered likely to contribute most to the advancement of the theory and practice of analytical chemistry. It is administered by the American Chemical Society and makes possible a year's work at a specified institution of higher learning in the U. S. or Canada. Dr. Byrne will continue research work, begun under the direction of L. B. Rogers, at MIT.

A grant of $10,000 has been made by the **American Cancer Society** to Joseph W. Beard, professor of experimental surgery, Duke University School of Medicine, for research in fowl leukosis. Dr. Beard, who has been working on chick tumor tissues, will attempt to isolate the virus that causes the cancerlike disease in chicks.

Rockefeller Foundation Grants for scientific work in the first quarter of 1950 have been made to the following institutions: *University of Heidelberg*—$56,000 for an institute of psychosomatic medicine, under the direction of Alexander Mitscherlich; *University of Copenhagen*—$63,000 for a child guidance clinic, under the direction of Bodil Farup, former Rockefeller Foundation fellow; *Medical Research Council of Great Britain*—$50,000 for fellowships in the medical sciences; *University of Cambridge, England*—$14,250 for research in neurophysiology, under the direction of E. D. Adrian; *Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine*—$150,000 for studies of genetic factors of intelligence and emotional variation in mammals (see *Science*, Feb. 17, p. 187); *Prince-*

ton University—$25,000 for studies of the psychology of perception by the Department of Psychology, in collaboration with Adelbert Ames, Jr., of the Hanover Institute, New Hampshire; *Stanford University*—$11,000 for continuation of a study of individuals who, as children (in 1921–22), scored unusually well on intelligence tests; *Columbia University*—$16,000 for studies in brain chemistry; *Medical Library Association*—$10,000 for fellowships in the U. S. for foreign medical librarians and $5,000 for shipment of extra copies of medical journals abroad; *Karolinska Institute, Stockholm*—$45,000 for research in biochemistry in the Medical Nobel Institute; *University of Stockholm*—$12,000 for research in biochemistry at the Wenner-Gren Institute and $4,200 toward expenses in research in radiobiology; *University of Virginia*—$30,000 toward research in the thermodynamics of enzyme action; *Harvard University*—$18,000 toward research in enzyme chemistry; *University of Washington*—$17,500 for an electron microscope for use in microanatomy research; *University of Tennessee*—$7,000 for research in biochemistry; *Michigan State College*—$10,000 for research in the field of plant biochemistry; *University of Chicago*—$9,000 toward research in animal ecology; *National Institute of Economic and Social Research, Great Britain*—$21,000 for the expenses of the International Association for Research in Income and Wealth; *University of Michigan*—$19,320 for studies of the validity and reliability of economic survey data and of basic determinants of economic behavior by its Survey Research Center and $52,500 for a program of methodological research in the field of human relations by its Research Center for Group Dynamics; *Food Research Institute of Stanford University*—$10,000 for Vladimir P. Timoshenko's research on food and agriculture in World War II, including a study of food and agriculture in the Soviet Union during that period, and $1,000 for a study of Yugoslav agriculture during the interwar period.

Rockefeller Foundation grants for the first quarter of 1950 total $1,254,433. This sum includes many grants-in-aid and a few grants in the humanities and other small grants not mentioned here.

The John Wesley Hyatt Award for 1950—a gold medal and $1,000—was presented to George M. Powell, III, technical head of Vinyl Coatings Research, Union Carbide and Carbon Corporation, at the annual meeting of the Society of the Plastics Industry, New York City. Dr. Powell received the award for his work in Vinylite dispersion resins.

The 1950 Knudsen Award of the American Association of Industrial Physicians and Surgeons was given to Edward Charles Holmblad, treasurer and managing director of the association. Dr. Holmblad has been active in the association since 1924.

Fellowships

The American College of Physicians has announced that a limited number of fellowships in medicine will be available from July 1, 1951 to June 30, 1952. These fellowships are designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in internal medicine. Applicants must be acceptable in the laboratory or clinic of their choice and be provided with necessary facilities. The stipend will be from $2,200 to $3,200. Application forms will be supplied on request to the American College of Physicians, 4200 Pine Street, Philadelphia, Pennsylvania, and must be submitted in duplicate not later than *October 1*. Announcement of awards will be made November, 1950.

The Arctic Institute of North America is offering a number of grants-in-aid for scientific work in the North American Arctic and Subarctic during 1951. Research must include field investigations either in Alaska, northern Canada, or Greenland. The grants are open to anyone who has demonstrated ability to conduct research work of superior quality in some field of science. Applications must be received by *November 1*. The awards will be made upon the recommendation of the Board of Governors of the Arctic Institute, and will be announced by March, 1951. Application forms may be obtained upon request to the secretary, Research Committee, Arctic Institute of North America, Baltimore-Washington Office, Rogers House, 3506 Greenway, Baltimore, Maryland.

Colleges and Universities

Cornell University has established a research laboratory for studies of infectious diseases of dogs. A new building, containing laboratories, office space, and isolation units for work on viruses, is being constructed as the second unit of a proposed animal disease research center, adjacent to a present building containing facilities for study of infectious diseases of farm animals, poultry, and cattle. Correlation of studies of diseases in different species of animals is planned, with particular attention directed to etiology and the prevention of disease. The new laboratories will be under the direction of James A. Baker, professor of bacteriology, New York State Veterinary College at Cornell.

The University of Notre Dame will hold a dedication program June 21 and 22 in connection with the opening of the Germ-Free Life Laboratories at the university's Laboratory of Bacteriology. Charles F. Kettering, director and research consultant of the General Motors Corporation, will deliver the principal address on the evening of June 21. A symposium, "Science and Society," will be held June 22. James A. Reyniers, director of the Laboratory of Bacteriology, will be chairman. Participants will include Charles DeKoniek, Laval University; Robert Chambers, New York University; Ira Baldwin, University of Wisconsin; Bradley Dewey, Dewey and Almy Chemical Company; Thorvald Solberg, Office of Naval Research;

Oram Woolpert, Chemical Corps; Watson Davis, Science Service; John H. Teeter, American Cancer Society; and Anthony Standen, Brooklyn Polytechnic Institute.

Summer Program

A laboratory course in the techniques and applications of the electron microscope will be given by the Laboratory of Electron Microscopy in the Department of Engineering Physics, College of Engineering, Cornell University, July 31–August 12. The course is designed for institutional and industrial research workers who have recently entered the field of electron microscopy or who are planning to undertake research problems involving applications of this instrument. Further inquiries should be addressed to Prof. Benjamin M. Siegel, Department of Engineering Physics, Rockefeller Hall, Cornell University, Ithaca, New York.

Meetings and Elections

The International Meteorological Organization's Committee for the Study of Clouds and Hydrometeors is meeting in Paris, June 12–24. The committee of eleven cloud experts hopes to complete the text and selection of photographs for a new International Cloud Atlas, which is used to promote uniformity of cloud reporting throughout the world. Charles F. Brooks, professor of meteorology and director of the Blue Hill Meteorological Observatory of Harvard University, is attending the meeting. Dr. Brooks is president of the Permanent Subcommission on Station Instruments and Exposures of the organization.

The American Veterinary Medical Association will hold its 87th annual convention in Miami Beach, Florida, August 21–24, with headquarters in the Municipal Auditorium. Further information can be obtained by writing to Dr. J. G. Hardenbergh, Executive Secretary, 600 South Michigan Avenue, Chicago.

The Seventh International Congress of Surgery will be held in Buenos Aires, August 1–5, under the auspices of the Argentine government. Carlos I. Rivas will be chairman. Contributed papers and U. S. representatives are invited. Information can be obtained from Exprinter S. A., San Martin 176, Buenos Aires, and All Nations Travel Bureau, 38 South Dearborn Street, Chicago.

The International Northwestern Conference on Diseases of Nature Communicable to Man will be held at the new School of Medicine, University of Washington, in Seattle, August 23–25. For additional information write to W. R. Giedt, Secretary, 1417 Smith Tower Building, Seattle, Washington.

The Tissue Culture Association has arranged a conference on tissue culture techniques and problems, to be held at Cooperstown, New York, August 31–September 2. These dates will be convenient for visitors in the U. S. who plan to attend the Seventh International Congress for Cell Biology at Yale University (*Science*, May 5, p. 505).

The American College of Physicians will conduct its 32nd annual session at St. Louis, April 9–13, 1951. Ralph Kinsella, of St. Louis, is the general chairman and will be responsible for local arrangements and for the program of clinics and panel discussions. William S. Middleton, president of the college, will be in charge of the program of morning lectures and afternoon general sessions. Secretaries of medical societies are asked to note these dates and, in arranging meeting dates of their societies, to avoid conflicts with the college meeting.

The Virginia Academy of Science has elected the following officers for next year: president, Guy W. Horsley; president elect, Paul M. Patterson; secretary, Foley F. Smith.

The Ohio Academy of Science elected the following officers at its annual meeting in Columbus, April 27–29: president, E. S. Thomas, Ohio State Museum; treasurer, R. M. Geist, Capital University; and secretary, Rush Elliott, Ohio University.

The West Virginia Academy of Science, at its annual meeting on May 5–6 elected the following officers for 1950–51: M. L. Vest, West Virginia University, Morgantown, president; N. Bayard Green, West Virginia University, vice president; E. E. Myers, Alderson-Broaddus College, Philippi, secretary; and James L. Hall, West Virginia University, treasurer.

The Eastern Psychological Association elected the following officers at its annual meeting, April 20–22: president, Carl I. Hovland, Yale University; treasurer, Wilbert S. Ray, Trinity College; board of directors, Harold Schlosberg, Brown University, and Frank Beach and Neal Miller, both of Yale University.

Deaths

William J. Dakin, professor of zoology at the University of Sydney, Australia, died April 2, at the age of 67. Dr. Dakin was known for his work in physiology and ecology of marine animals, and in oceanography.

Charles Edward Skinner, 84, died May 12 in San Mateo, California, while visiting his daughter. Dr. Skinner, an electrical engineer, was the first director of research for Westinghouse Corporation, and had served the firm 43 years when he retired in 1933.

Fred A. Barnes, 73, died April 5 at his home in Pleasant Valley, Connecticut. Dr. Barnes was professor of civil and rail engineering at Cornell University for 44 years, until his retirement in 1946.

Miscellaneous

Music with anesthesia has been installed in the University of Chicago clinics to help alleviate tension of patients undergoing surgery. Used with spinal, local, or regional anesthesia, the music is piped to the operating rooms from a central recorder room where three duo-channel magnetic tape recorders of

classical, semiclassical, and popular music play continuously for four hours. The patient and the anesthesiologist, who proctors the program, hear the music through lightweight stethoscope-type earphones.

Music for surgery is not a new idea. Surgeons have reported in medical literature on the success of the use of phonograph and radio in operating rooms. It was first introduced in the University of Chicago clinics in 1947 as a research experiment, financed by a grant from the U. S. Navy, and proved so successful that funds were raised by Maurice Goldblatt, president of the University of Chicago Cancer Foundation, for a permanent installation. The program is under the direction of Lester R. Dragstedt, chairman of the university's Department of Surgery. The Nathan Goldblatt Memorial Hospital, formally dedicated on June 15, will use music with anesthesia in its six major operating rooms and six preparation rooms.

Proceedings of the Second Conference on the Biology of Normal and Atypical Pigment Cell Growth, held last November, were recently published in *Zoologica* and have been reprinted in a 32-page booklet. Those interested in pigment cell problems may obtain copies on request to Dr. Myron Gordon, Genetics Laboratory, New York Zoological Society, American Museum of Natural History, New York City.

The Pacific Science Council (*Science*, May 26, p. 564) established its permanent secretariat in Honolulu, March 20. Loring G. Hudson, the executive secretary, may be addressed at Bishop Museum, Honolulu 17, T. H.

A two-volume bibliography on audition, including some 5,500 titles, has been compiled by the Psycho-Acoustic Laboratory of Harvard University under contract with the Office of Naval Research. The bibliography is supplemented by a topical index that lists the authors under six major headings: basic references, the anatomy of the ear, the physiology of the ear, the psychology of hearing, deafness, and theories of hearing. The principal abstracting journals relied upon were *The Journal of the Acoustical Society of America, Psychological Abstracts,* and *Index Medicus.* A limited number of copies are available from the Harvard University Press, Cambridge, Massachusetts, at a price of $3 for the two volumes.

A cancer research program for the study of treatment of neoplasms through use of radiation from radioactive isotopes, conducted by the Medical Division of the Oak Ridge Institute of Nuclear Studies in cooperation with 23 southern medical schools, will be in full operation July 1. A 30-bed clinical unit, laboratories, treatment rooms, and radiation storage facilities have been constructed. Patients will be selected for treatment by the participating medical schools only and no patient will be considered if the neoplastic condition is amenable to surgery or x-ray therapy. Members of the Medical Division staff are: Marshall Brucer, chairman; H. D. Bruner, principal scientist; Gould A. Andrews and Jesse D. Perkinson, senior scientists in hematology and biochemistry; and E. R. King, of the Navy Medical Corps.

The American Research Center in Egypt, established last year, will be opened in Cairo early in 1951 for study of civilizations in the Nile River area. It will serve scholars and qualified U. S. students as a research and teaching center, in a manner similar to that of other American schools already established in Rome, Athens, Baghdad, Jerusalem, and North Africa. The older schools will aid the work of the new center, Chicago's Oriental Institute will make available its library in Luxor House, and the Egyptian, Coptic, and Arabic Museums, as well as the National Library and the French Institute Library in Cairo, will be open to the center. Edward W. Forbes, director emeritus of the Fogg Art Museum of Harvard University, is president of the American Research Center, and Sterling Dow, professor of history and Greek at Harvard, is secretary. William S. Smith, of the Museum of Fine Arts in Boston, will be director of the center in Egypt for 1950–51.

Make Plans for—

American Meteorological Society, 107th national meeting, June 21–23, Salt Lake City, Utah.

American Physical Society, 300th meeting, June 21–24, Mexico City, Mexico.

American Association of Petroleum Geologists, regional meeting, June 22–24, Charleston, West Virginia.

Acoustical Society of America, annual meeting, June 22–24, State College, Pennsylvania.

American Heart Association, annual meeting, June 22–25, Fairmont Hotel, San Francisco, California.

American Society for the Study of Sterility, June 24–25, Sir Francis Drake Hotel, San Francisco, California.

American Optometric Association, June 25–28, Minneapolis, Minnesota.

American Society of Mammalogists, annual meeting, June 26–29, Mammoth, Yellowstone National Park.

Recently Received—

A Progress Report on Cortisone. Merck & Co., Rahway, N. J.

Survey of Power Sources. Vols. 1–3. Library of Congress, Photoduplication Service, Publication Board Project, Washington 25, D. C. $9, $7, $8, respectively.

Australian Environment. Tait Book Co. Pty., Ltd., 349 Collins St., Melbourne, Australia. 10s.6d.

Carnegie Institution of Washington Year Book, No. 48, 1948–49. Carnegie Institution of Washington, Washington 5, D. C.

English Index to Soviet Medical Periodicals. Vol. 1 1945–47. Donovan T. Richnell. H. K. Lewis and Co., Ltd., London, England.

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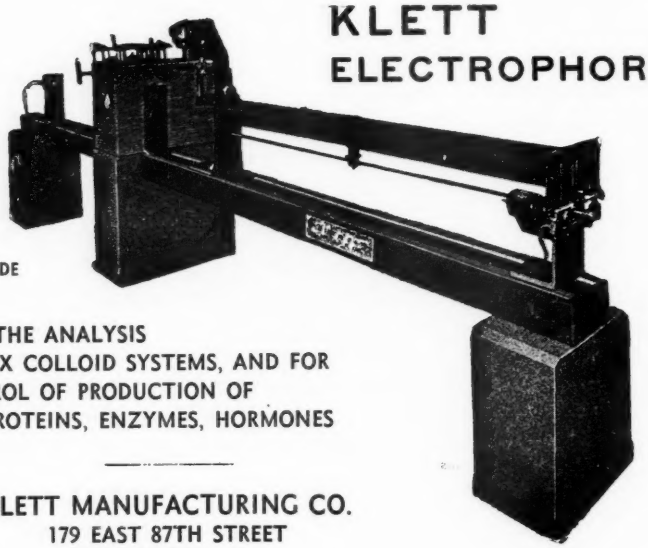

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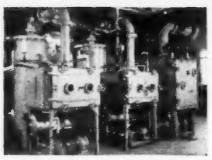

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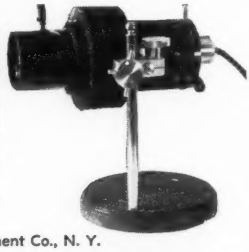

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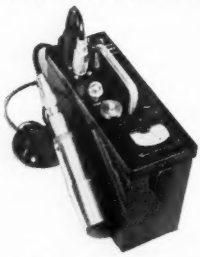

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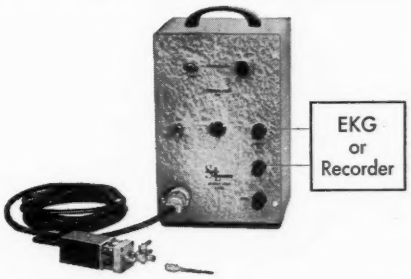

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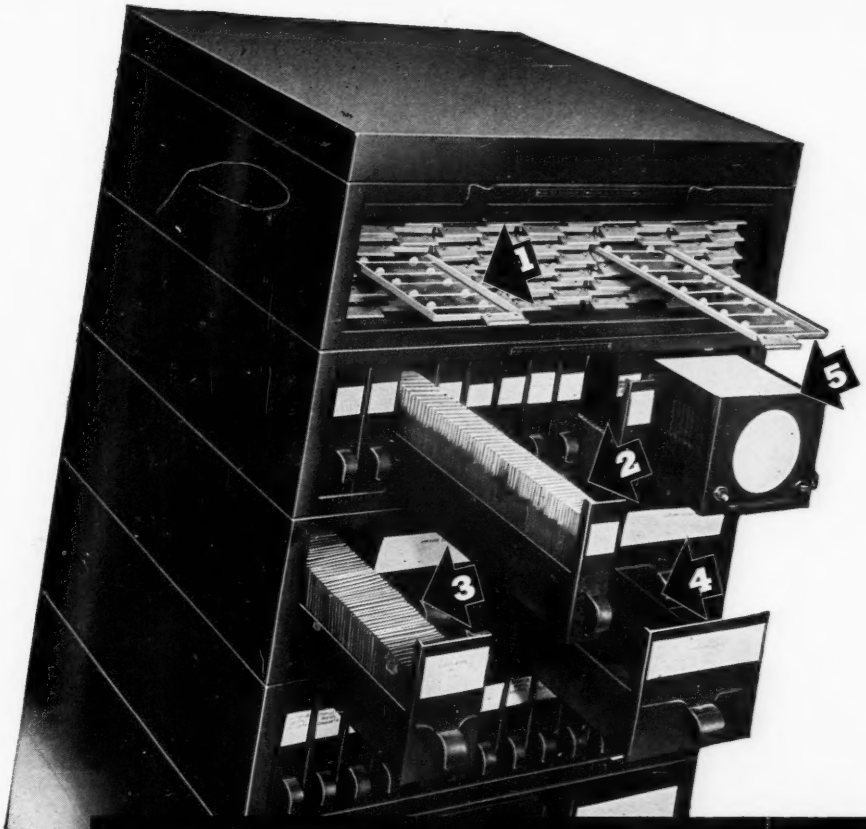

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